



THE  
SURGICAL CLINICS  
OF  
NORTH AMERICA

*Frank L. Norvell.*

APRIL, 1927

VOLUME 7 — NUMBER 2

CANCER

II

PHILADELPHIA AND LONDON

W. B. SAUNDERS COMPANY

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SQUARE PHILADELPHIA

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# THE SURGICAL CLINICS OF NORTH AMERICA

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Volume 7

Number 2

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CLINIC OF DR JOHN BERTON CARNETT

GRADUATE SCHOOL OF MEDICINE UNIVERSITY OF PENNSYLVANIA

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## ETHYL CHLORID AS A LOCAL ANESTHETIC FOR TAKING BIOPSIES AND OPENING ABSCESSES

THIS man is fifty eight years of age and for the past eight months has been developing this atypical ulcer on the front of his neck. The clinical diagnosis is uncertain and our purpose in bringing him before you is to remove a bit of tissue to establish a *microscopic diagnosis*. In the sitting position the patient's head would be unsteady and the lesion rather inaccessible hence we have him brought in on the table with his shoulders elevated on a flat sand bag in order to extend his head. We scrub our hands and put on sterile rubber gloves. We next proceed to drape sterile sheets about the field of operation using one of them to cut off the patient's view of the proceedings which is always desirable with any local anesthetic but particularly so in using ethyl chlorid about the head in order to avoid accidentally spraying it into the eyes.

We will now dry off the secretions with a gauze swab and then paint the surrounding skin and ulcer with a 2 per cent solution of mercurochrome. In passing I might mention that irritating solutions such as iodine picric acid etc should not be used wherever there is a possibility of irradiation being required, as the skin cannot withstand the double irritation. I am using 3 per cent mercurochrome as a skin disinfectant in all my operative work and find it very satisfactory.

We have not acquired the brutality necessary to cut through

sensitive skin without an anesthetic in making biopsies. We have tried various local anesthetics and about a year ago we came back to ethyl chlorid as being the safest and simplest. Ethyl chlorid is the safest anesthetic to use because the freezing of the tissues tends to fix the cancer cells *in situ* during the subsequent manipulation and thereby lessens the danger of embolism.

If you will pardon another digression I want to repeat to you a statement made recently by Mr W. Sampson Handley while he was here in Philadelphia. I had told him we had not had much luck in finding permeated cells in the lymphatics on the deep fascias. He then explained a step in his technic of removing strips of skin, fat, fascia and muscle from the chest and abdomen which he does not mention in his book on *Cancer of the Breast*. He cuts a strip from the cadaver three times as wide as he needs using a very sharp knife and carefully refraining from exerting any pull or pressure which might dislodge the cancer cells. This strip is immediately frozen and only then is it cut into three strips, the central one only being reserved for study. He has found that the act of cutting the central strip only directly from the cadaver results in emptying it of the great majority of its cancer cells. I have asked our pathologist to check up on this statement because if true it indicates the necessity of using even greater gentleness than we have been accustomed to teach our students and to practice ourselves both in palpating and in operating for cancer and it may even demand a revision of our operative technic in some forms of cancer. In the meantime in using a local anesthetic we feel better satisfied that we are less apt to dislodge cancer cells by freezing than by injecting solutions in making a biopsy.

We will now return to the business at hand. Our surface is dry otherwise we would gently mop it off. I make sure that a sharp knife is within easy reach. The type of ethyl chlorid container (Fig. 154) with its regulating screw valve is greatly to be preferred to the type (Fig. 155) which cannot be regulated and which shoots such a coarse stream that it is difficult to produce anesthesia even when the container is held at a distance.

The unevaporated fluid is apt to flow into the eyes, mouth, or other objectionable regions, and this apparatus, being wasteful, is correspondingly more expensive.

An intern is available to spray the ethyl chlorid, otherwise I would use it myself. He advances the nozzle to within 2 or 3 inches of the lesion and keeps the bottom of the container at

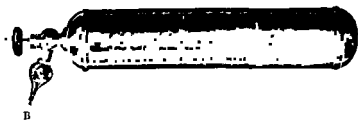


Fig. 154 —Metal container A, Valve regulator, B, glass nozzle

a higher level than the nozzle. By holding the body of the container between his palm and last three fingers, his index-finger and thumb of the same hand will be free to turn the regulating valve to a point where such a fine spray will be ejected that it will evaporate as rapidly as it meets the skin without any surplus flowing away. It is much more difficult to hit the target with an unregulated coarse spray as it has to be held 12 to 18 inches

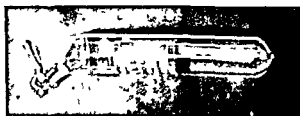


Fig 155 —Glass container without regulating valve

away in order to secure evaporation at the skin surface, and even then much of the solution drains away from the operative field before it evaporates. Recognizing the above difficulties some of the manufacturers of ethyl chlorid continue in this aseptic age to send out in each package printed advice that must have come down from pre-Listerian days to the effect that the surgeon should blow on the operative field in order to expedite evapora-



tion Although ulcers for biopsy or abscesses for incision do contain relatively harmless staphylococci there seems no good reason for the surgeon to create a virulent mixed infection by blowing his breath and particles of saliva containing streptococci and pneumococci the bacilli of diphtheria or tuberculosis or any other vicious germs over the proposed site of excision or incision

The intern will now proceed with spraying the area I am outlining and in a few moments it will turn white indicating that the surface is frozen but he will continue the spray a little longer to secure deeper freezing He now withdraws the spray and I promptly remove a thin strip of tissue which includes some of the ulcer the edge of the ulcer and some of the adjoining skin This excision is accomplished by two gentle knife strokes that converge to meet a short distance beneath the skin while my left thumb and finger steady the adjacent tissues We turn this specimen over to the pathologist who will make a frozen section immediately Were we to send the specimen to a pathologist in another city we would place it in a 10 per cent solution of formalin at once and send specimen and solution to him While talking to you I swabbed out my small incision with 2 per cent mercurochrome We apply sterile gauze and a bandage over the ulcer and return the patient to his ward

This patient was shown at the weekly conference of the entire radiologic staff and no one thought the lesion was cancer otherwise we would have obtained permission from the patient to do a radical operation at this time and if the frozen section showed cancer we would then have given him gas oxygen anesthesia and proceeded with the operation instead of letting him return to the ward We find the ethyl chlorid anesthesia method for removing biopsies conserves the surgeon's time and shortens the duration of the general anesthetic in the event of a radical operation proving necessary An intern takes the biopsy and turns it over to the pathologist for frozen section diagnosis about one half hour before the surgeon is ready to operate

I have found ethyl chlorid very satisfactory as a local anesthetic for incision of superficial abscesses The freezing itself

may cause some pain in very acute abscesses, but the incision itself need not cause any pain if the simple precaution is taken to make only the very gentlest pressure with a sharp knife edge.

By reference to the diagram (Fig. 156) it becomes obvious that freezing will anesthetize the tissues at *A-B-C* overlying the abscess, but will have no effect in abolishing sensation in the inflamed tissues beneath the abscess at *A-D-C*.

By making only light gentle strokes with the sharpest, thinnest bladed knife obtainable it is possible to cut through anesthetized *A-B-C* without causing any pressure on hypersensitive *A-D-C*, and consequently there will be no pain. I frequently use

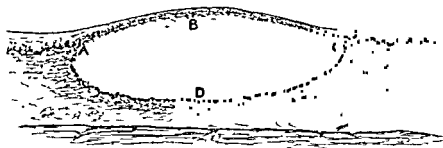


Fig 156 —Subcutaneous abscess. After spraying with ethyl chlorid *A-B-C* is anesthetic, but *A-D-C* remains hypersensitive

four or five strokes in the same groove in cutting through the skin.

I was on the verge of abandoning ethyl chlorid several years ago, but I then tried out the above principles, and have been using it frequently as a local anesthetic ever since. I am fortunate in having a friend who is an ophthalmologist and uses each of his cataract knives only once and then presents them to me. They are ideal knives when properly sharpened for opening abscesses by this method.

The usual practice in opening an abscess is for the operator to doubt the efficiency of the ethyl chlorid anesthesia, and knowing that freezing has toughened the skin he tries to finish his disagreeable task by one fell swoop of a knife which usually has not been sharpened within the past ten years. Whether the

incision has been made from without inward or from within outward after first thrusting the knife into the abscess, the resulting pressure or traction on the *A-D C* tissues will provoke intense pain

Because of its compactness and ease of administration by the operator himself ethyl chloride has come to occupy a prominent place in my office and visiting bag

Here comes the pathologist, and he tells us that his frozen section examination shows that our patient's neck lesion is due to tuberculosis

## AN ATYPICAL CANCER OF THE FOREARM WITH DISCUSSION OF THE BIOPSY QUESTION

THIS young man is a laborer, twenty-four years of age. Twenty months before admission his right forearm was spiked by a fellow player's baseball shoe. The wound remained open and after one week began to suppurate and then slowly but steadily



Fig. 157.—Ulcer with everted edges surrounding two-thirds of forearm

increased in size. He did not consult any physician, but treated the wound with home remedies until one year ago, when he was admitted to the surgical service of this hospital. The surgeon on duty advised amputation, but the patient refused. A biopsy taken at that time was negative for cancer. The lesion was treated with antiseptics for six weeks and then the patient left

the hospital. One month later he returned and was admitted to my service in the Radiologic Department. The lesion as it then appeared is shown by this photograph (Fig 157). The large ulcerating lesion had destroyed the extensor tendons. The wrist and finger joints were fixed in flexion. The radius and ulna

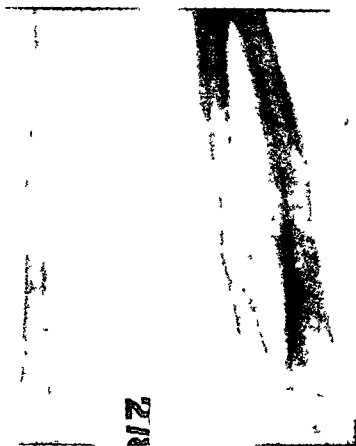


Fig 158—Cancerous invasion bones of forearm

were exposed in the bottom of the ulcer and both showed evidence of a destructive process (Fig 158). The ulcerating surface bled easily and it was surrounded by an elevated indurated everted skin margin. One small epitrochlear lymph node and several larger moderately firm axillary nodes were palpable. This

young male adult was otherwise in good physical condition. His Wassermann test was negative. He had no leukocytosis.

Clinically the lesion was typical of cancer, but repeated liberal biopsies through the ulcer margin at various parts of its circumference failed to confirm that diagnosis. The microscope revealed only chronic inflammation without evidence of tuberculosis, syphilis, or any other specific disease process. Smears and cultures from the wound showed a few hemolytic streptococci with *Bacillus proteus* and a diphtheroid bacillus present in large numbers. An active bacteriologic search was made for unusual microorganisms, but none were found. Acting on the assumption that the lesion might be due to chronic inflammation, kept up by bacteria buried in the depths of the ragged lesion, the patient was advised to have an electrodesiccation to destroy the surface tissue and sterilize the ulcer. On the operating table this plan was changed because the typical cancer appearance created a desire to obtain more tissue for pathologic study. An extensive débridement of the entire ulcer surface and skin margins was performed without any desiccation. Numerous microscopic slides were prepared from this tissue, but the pathologists could not agree on a diagnosis. The majority of the slides showed only inflammatory changes, but from the depths of the wound entirely away from the skin margin some tissue was found that was suspicious of malignancy. The same set of slides (Figs. 159, 160) were examined by various eminent pathologists. I take the liberty of mentioning three of them by name, viz., Dr. Allen J. Smith, Dr. Joseph McFarland, and Dr. Joseph C. Bloodgood, but I am not confiding to you the particular diagnosis made by each one. Suffice it to say that the diagnosis by one of them was chronic inflammation without malignancy, by another was carcinoma, and by a third was sarcoma originating in the granulation tissue of a chronic ulcer. As a clinician, who is not infallible in diagnosis, I take great comfort at times in finding that pathologists do not always agree on the interpretation of the picture they see under the microscope.

Following the débridement one surface application of radium was applied to the lesion, without noteworthy result. The

experience with cancer in young people indicates that it occurs most frequently in the rectum. I have seen several cases of rectal carcinoma in patients in their early twenties and in none of them because of their youth was the nature of the lesion suspected until it became inoperable.

The location of the lesion on the mid forearm was somewhat unusual as skin cancer is far more common on the uncovered skin surfaces of face, neck, and hands.

A very interesting feature was the development of cancer in a wound which never healed although it was located in a region in which a good blood supply normally ensures prompt healing. I suspect the cancer developed because the prolonged suppuration without proper surgical treatment acted as a chronic irritant to the epithelial edges of the wound. I blame the origin of the cancer on the infection rather than on the trauma. It seems almost incredible that anyone as seemingly intelligent as this patient and living in Philadelphia with its multitude of physicians and surgical clinics should refrain from seeking professional advice about his wound for a full eight months. I have frequently speculated as to whether or not proper surgical attention in the early days of that injury would have prevented cancer and I incline to the belief that control of the infection would have prevented the neoplasm.

We have had on the radiologic service a similar case of a traumatic wound with prolonged suppuration in which cancer developed. A woman fifty years of age sustained a lacerated wound of the scalp in an automobile accident. She was confined in a hospital for twelve days for treatment of her infected sloughing scalp wound. She thereafter drifted from one physician to another but the wound never healed. She came to us four and one-half years after her accident. She then had a far advanced basal cell carcinoma 4 by 6 inches in size over the vault of the skull (Fig. 162). The skull was extensively eroded exposing one large and several small areas of pulsating dura. She had marked secondary anemia due to persistent bleeding. Under repeated applications of radium the bleeding was checked and her hemoglobin rose from 30 to 68. The cancer showed definite

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on his enlarged axillary lymph-nodes. The amputation above the elbow was done five months ago. Further pathologic studies proved inconclusive. Our indefatigable Resident Pathologist, Dr. J. L. Goforth, returned from his summer vacation about this time and he retackled the baffling problem of establishing a decisive diagnosis. He discovered the epitrochlear node in the amputated member and slides from it showed unmistakable evidence of metastatic squamous-cell carcinoma (Fig. 161).

The patient's convalescence from the amputation was uneventful and you will note that he now has an excellent stump. The

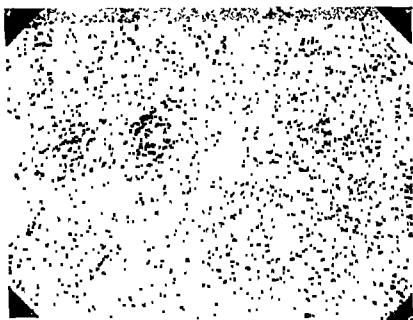


Fig 161 —Microphotograph of epitrochlear lymph-node

axillary nodes are somewhat smaller than on admission to my service eight months ago. Their enlargement may be due either to chronic infection or neoplasm, or to both. We believe they have been invaded by cancer, but he still declines to have them removed and they are being treated by radiation.

There are several points worthy of further comment in connection with this case. In the first place, the patient was rather young for skin cancer, as he had barely reached his twenty-fourth birthday when he sustained the injury to his forearm. My

experience with cancer in young people indicates that it occurs most frequently in the rectum. I have seen several cases of rectal carcinoma in patients in their early twenties and in none of them because of their youth was the nature of the lesion suspected until it became inoperable.

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surface improvement during the eighteen months she was under treatment. Her only brain symptoms consisted of a convulsive seizure two days before her death which followed a severe hemorrhage from the longitudinal sinus. I believe the prolonged infection rather than the original trauma was the activating cause of her cancer. These 2 cases of cancer developing in recent unhealed traumatic wounds are unusual.



Fig 162 —Basal cell carcinoma originating in a scalp wound

Male patients frequently tell us that their cancers of the face resulted from one or more razor cuts, but in such instances as a rule the cancers antedate the razor injuries.

It is fairly common to see cancer develop in the scars of past wounds and burns or in the margins of chronic ulcers, such as occur on the leg or as a result of syphilis or tuberculosis.

Attached to our forearm patient's record are over seven pages of pathologic notes dealing with this ulcer. These notes were made in part by our hospital's pathologic staff and in part

by pathologists in New York and Baltimore who have very generously cooperated in studying the specimens of our puzzling cases

It is most unusual for pathologists to express such diverse views in cases similar to this ulcer of the forearm, particularly as the entire lesion was finally available for their study. They are more apt to differ with one another on their interpretations of microscopic slides from cases of endotheliomata, malignant melanotic tumors and tumefactions of lymph nodes. It is interesting to note in the lesion under discussion that no cancer cells were found anywhere along the skin margin. This case is therefore an exception to the general rule that the most vigorous and typical cancer cells are found at the periphery of the lesion whether it be primary or metastatic.<sup>1</sup>

It was with some reluctance that I brought this patient before you because I did not want to prejudice you against biopsies which as a rule are the most reliable means of establishing a correct diagnosis in cases of suspected malignancy. This case demonstrates that a biopsy report especially if negative for malignancy is like any other laboratory report or clinical finding in that it needs to be weighed carefully in the balance when it conflicts with other evidence.

The usual cause of a misresult is faulty selection of the biopsy material. An inexperienced intern is prone to select tissue that can be removed with least discomfort to the patient, and that commonly means the biopsy consists of a protruding knob from

<sup>1</sup> Shortly after being shown in the clinic the patient terminated his visits to the radiologic department. Six months later he was admitted to Dr. Loewenburg's medical service in this hospital and died five days later. The autopsy findings of Dr. J. L. Goforth contain the following points of interest. Metastatic squamous carcinoma as shown by the microscope was found in (1) Three nodules involving skin, fat and fascia located respectively over left temple, right chin and central scalp; (2) the right axillary, peribronchial and peripancreatic lymph nodes; and (3) nodules mainly on surface of the lungs but also scattered through their substance. The immediate cause of death was widespread acute bronchopneumonia and bilateral fibrinous pleurisy. After studying the original and autopsy slides Dr. James Ewing of New York City confirmed the diagnosis of squamous cancer and stated the cells are quite anaplastic and therefore lack some of the squamous-cell characteristics.

the central atypical portion of the ulcerative lesion. Under such circumstances the pathologist's labors are apt to be wasted and another biopsy will be in order. The pathologist in his laboratory clamors for a maximum of tissue, whereas the surgeon in dealing with the living patient is prone to remove only a minimum. It is sometimes amazing how small a biopsy will suffice. For instance, in cancer of the esophagus tissue the size of a safety match head commonly leads to a positive microscopic diagnosis, but if not the biopsy should be repeated.

In accessible ulcerative lesions of skin or mucous membranes it is much safer to make larger biopsies which should include a thin slice of (1) a portion of the ulcer; (2) the margin of the ulcer; and (3) a portion of the adjacent skin or mucosa. Much has been written about the danger in making biopsies of opening up blood-vessels and lymph-channels, thereby permitting cancer cells to migrate to distant points. There is no doubt this danger does exist, but with proper safeguards I believe it is very slight.

The use of a cautery knife in making a biopsy seals the vessels as they are divided, but conscious patients object to the odor of their own burning flesh and the specimen removed has to be larger because of the charring of its cut surfaces. For conscious patients, a sharp knife used gently with local ethyl chlorid anesthesia is very satisfactory (see p. 238).

A biopsy is the most valuable means of determining the diagnosis in the doubtful ulcerative lesions of the skin and accessible mucous membranes. The blood-vessels encountered at their margins are usually insignificant.

If the lesion is small it should be removed *in toto* together with a margin of healthy tissue surrounding it, in which event the excision may be both diagnostic and curative.

Precancerous lesions should be excised unless undue deformity—as in the region of an eyelid—would result, in order to determine not only whether malignancy has occurred, but if so whether it is of a basal-cell or prickle-cell variety. Primary treatment of these cases by radiation leaves in doubt both the diagnosis and the need for follow-up and future treatment.

Even in cases of fairly typical ulcerative cancer I am in the habit of checking up the clinical diagnosis by a biopsy before resorting to an extensive or mutilating operation as in cancer of the tongue or rectum. I am very reluctant to resort to biopsies on more deeply situated cancers because of the danger of metastasis incident to dividing numerous blood and lymph vessels. When I am reasonably sure of the diagnosis of cancer in the deeper tissues as of the breast or parotid gland I usually prefer to do the radical operation without running the risk of making a biopsy.

As a rule biopsies should be rigidly avoided in sarcomata because of the large thin walled blood sinuses in them favoring distant blood stream metastases and because of their tendency to fungate through the biopsy incision. I make an exception to this rule in the cases in which amputation is contemplated for bone sarcoma. Having gained the patient's consent to amputation a tourniquet is applied to the extremity immediately above the tumor. An incision is then made into the tumor to remove tissue for frozen section diagnosis. If the microscopic study negatives the need for amputation the limb can be saved. If amputation proves necessary the original tourniquet is kept *in situ* to prevent any malignant cells escaping while the limb is divided at a higher level.

The therapeutic effect of radiation is often helpful in arriving at a diagnosis in some cases of suspected sarcomata. When the history, clinical findings and blood picture fail to establish a diagnosis in cases of enlarged lymphatic glands a small outlying gland should be removed in its entirety for microscopic examination. A biopsy in these gland cases is especially important because the radiation dosage that exerts a favorable influence in one disease may prove disastrous in another.

The ideal arrangement is to have the patient in the hospital and ready for whatever curative operation is necessary before taking any biopsy so that in the event of a frozen section diagnosis proving positive for cancer the radical operation can proceed at once. This ideal plan is insisted upon for all deeply situated uncertain but suspected cancers. It is not so imperative for the

superficial ulcerative lesions, especially so if the probability is against cancer being found by the biopsy. Patients generally give consent more readily and at an earlier stage for a biopsy than can be obtained in office or clinic and that does not require their admission to the hospital. This is particularly true of patients who live at a considerable distance from hospitals. A biopsy proving positive for malignancy under these circumstances justifies the physician's demand that the patient must enter the hospital at once for radical treatment.

I teach medical students that cancer should be treated as a semi-emergency, and that in any case in which it is suspected measures should be taken to establish an immediate diagnosis. The students are advised to suspect cancer in any ulcer that persists for three weeks on any mucous or skin surface—except between the knee and ankle. The general practitioner is all too prone to indulge in the pernicious use of the silver nitrate stick on early cancerous ulcers, and when healing does not occur after some weeks he next suspects syphilis and has a Wassermann test made. If the test proves positive, valuable weeks or months are lost in treating the patient for syphilis. The general practitioner should realize that the presence of syphilis does not render the patient immune to cancer. In any doubtful ulcerative lesion a biopsy should be the first step to settle the diagnosis. A biopsy will settle the question of cancer and tuberculosis and it may show evidence of syphilis. A Wassermann test may be taken coincidentally or subsequently, but it should never be relied upon to exclude cancer. I urge our students to take a biopsy in a suspected ulcer at the patient's first or second office visit (*i. e.*, within twenty-four hours of first seeing the patient) and then if malignancy is found the patient must be sent to the hospital within the next forty-eight hours. This routine procedure is far less dangerous than the alternative of having the patient return for examination week after week awaiting the development of characteristic cancerous manifestations. Although cancer grows more rapidly than benign lesions yet its growth is essentially slow, and whether situated on the surface or in the deeper tissues, it may not show any material change in many weeks, but



in the meantime an insidious embolism may have carried the disease far beyond the limits of the operative field. We never know on what day or hour a cancerous embolism may occur hence the great need for early diagnosis and immediate treatment of all cancer cases. Prolonged delay in diagnosis and repeated weekly palpations of cancerous lesions is far more likely to result in the embolic spread of cancer than is the early resort to routine biopsies.

Knox<sup>1</sup> has demonstrated that gentle massage of mouse tumors expedites distant metastases. Repeated palpation especially if not carried out with the utmost gentleness, may be expected to result in similar harm in human cancer.

<sup>1</sup> Knox Leila C. *Annals of Surgery* February 1922

## THE ACQUIRED SENSORY NERVES OF THE COLON AND DUODENUM

ORDINARILY the large and small intestines are not supplied with nerves of pain sense and any part of the intestine can usually be incised or resected without pain although manipulation or resection of its meso is painful

About three years ago my attention was very forcibly directed to the fact that division of the large intestine may be very painful. At that time I performed a Mikulicz multiple stage resection of the hepatic flexure on a physician. Division of his ascending colon one week after the primary operation caused great pain, but division of the transverse colon was painless. I have encountered only a few additional instances in which the large intestine seemed to be supplied with sensory nerves.

The presence or absence of sensory nerves in the large intestine is dependent upon the changes that take place in the meso colon before birth.

I described these prenatal alterations in the mesocolon in an article from which I will quote on Inguinal Hernia of the Cecum<sup>1</sup>

'A study of its development explains the variations in the anatomical relations of the ascending colon. For a time during early fetal life the greater part of the intestines lie within the umbilical cord, but between the seventh and ninth weeks they are drawn into the abdominal cavity. At this time the entire great intestine lies to the left of the median line. With the superior mesenteric artery as an axis the cecal end of the large intestine passes upward to the cardiac end of the stomach across under the liver, and finally downward to reach the right iliac fossa about the eighth month of intra uterine life.

'During its period of development the ascending colon is provided with a mesentery, attached to the spine in common with the small intestine. This primitive ascending mesocolon

permits great mobility of the colon and may persist in adult life as in 2 cases out of 100 autopsies reported by Treves

In the great majority of cases however the ascending colon loses its primitive mesocolon before birth and gains a secondary attachment to the posterior abdominal wall in the right lumbar region by a process of fusion (Fig 163) between the posterior parietal peritoneum (E D) and the superjacent leaflet of the primitive mesocolon (A B) These two peritoneal layers then

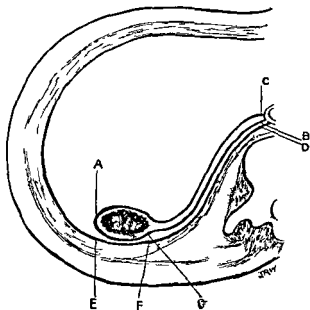


Fig 163 —Primitive mesocolon (Modified from Persol's Anatomy)

degenerate forming areolar tissue or a thin fascial layer and lose their identity as serous structures and that leaflet of the primitive mesocolon (A C) which originally faced toward the median line (anterior leaflet) becomes the posterior parietal serous covering The ascending colon at this stage has acquired a position which heretofore has commonly been called retroperitoneal In the newborn always and in the adult usually after breaking through the line of adhesion between the anterior leaflet of the primitive mesocolon and the lateral parietal peri

toneum at the outer border of the colon (A, E), it is possible to separate the two fused layers and reestablish the primitive mesocolon. Some modern anatomists maintain the view that the colon is never extraperitoneal, inasmuch as there exist two fused peritoneal layers between this viscus and the posterior abdominal wall. The interpretation of the term 'retroperitoneal' has served as a constant source of contention between the surgeons and the anatomists who have discussed cecal hernia. It therefore seems wise to reserve the terms 'retroperitoneal' and 'extraperitoneal' for those viscera (as kidneys, ureters, bladder, etc.) which while lying in partial contact with the peritoneum, were never surrounded by it, and to employ the terms 'retroserous' and 'extraserous' for those viscera (as ascending and descending colon, duodenum, pancreas, etc.) which at one time, for all practical purposes, might be considered as having been completely intraperitoneal, but which by fusion have lost their serous layer on one or more aspects. These terms will be employed with the above meaning in the remainder of this paper.

"After the primitive ascending mesocolon becomes lost by fusion the colon is held in fairly close contact with the posterior abdominal wall. It may retain this position, or in later life the peritoneum at either side of the colon may elongate and form the adult or definitive ascending mesocolon."

Fusion of the primitive mesocolon with the posterior parietal peritoneum with or without the later development of a definitive mesocolon may occur with the descending colon and sigmoid the same as with the ascending colon.

The parietal peritoneum or its adjacent fat contain an abundance of sensory nerve terminals connecting with the spinal cord. The visceral peritoneum is free from sensory nerves. The colon is never supplied by pain sensory nerves through the primitive mesocolon. The only portions of the intestine which acquire sensory nerves are those portions which fuse with the posterior parietal peritoneum so that the latter with its contained sensory nerve supply becomes to all intents and purposes an additional layer or coat of the intestine. The only sections

of the intestine which commonly undergo fusion to the parietal peritoneum to any extent are the posterior aspect of the duodenum and of the ascending descending and sigmoid colon

By reference to Fig 163 it is obvious that the colon will not acquire sensory nerves from the parietes when fusion between the primitive mesocolon (A B) and parietal peritoneum (D E) is limited to the sections G B and F D It is also apparent that the colon will acquire parietal sensory nerves to whatever extent fusion occurs between the peritoneum covering its posterior wall (A G) and the parietal peritoneum (E F) It is likewise evident that any acquired nerve supply will be limited to the posterior half of the colon

If a definitive mesocolon should develop the colon tends to rotate inward so that its original posterior surface faces away from the midline of the body I have had one previous case of colostomy in which the outer half circumference of the exposed loop of sigmoid was sensitive to pin pricks and the inner half circumference was entirely insensitive and I will now demonstrate another similar case to you

This patient has an inoperable adenocarcinoma of the rectum for which the first stage of a left iliac colostomy was done one week ago We have not opened the colostomy loop heretofore because the fecal current has continued to pass through it as evidenced by frequent stools every day and by lack of abdominal distention

We will shut off the patient's view of her wound by heaping up one of the sterile sheets You will now observe a pin can be pushed entirely through the wall of the mesial half circumference of the exposed sigmoid at various points without causing any distress whereas even superficial pin pricks at every point over the outer half circumference of sigmoid or over the inner or outer leaflet of the mesosigmoid cause pain The outer semicircumference of the sigmoid obtained its sensory fibers by fusion with the posterior parietal peritoneum We intend to remove a 2 inch section of this exposed gut and have a study made of its nerve supply In order to avoid pain it is necessary to produce local anesthesia by infiltrating the exposed definitive mesocolon with

a  $\frac{1}{2}$  per cent solution of novocain. Pricking and scratching of the previously sensitive gut is now painless. If the patient were under a general anesthetic and therefore could not smell her own burning flesh we would use some form of cautery to divide the gut. In this instance we will use a scalpel, even though it entails a little more trouble in grasping and tying blood vessels.

Dr G. L. Goforth made several beautiful sections showing the entire circumference of the sigmoid on each slide, but he found such extensive inflammatory changes had occurred in the exposed gut that he was unable to demonstrate any nerves or nerve terminals.

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to have heavy colds during the winter and has not felt well since Six weeks before admission he began to have lightning like abdominal pain which he said made him short of breath The pain was associated with nausea but no vomiting, and apparently was not related to taking of food One month before admission he began to have attacks of precordial pain, radiating across to the other nipple His appetite was variable, but his digestion always poor, with nausea and constipation He said he had lost a great deal of weight and on admission only weighed 120 pounds He coughed a great deal, but never any blood His ankles were edematous He had frequency of urination and nocturia (4-5)

His past and family history were of no importance

On physical examination he seemed much emaciated and anemic There were a few hard lymph nodes palpable in the neck The lungs showed increased fremitus and decreased expansion at the left apex and rales and dulness at the right base The enlarged heart had a systolic murmur at the apex and the aortic region The liver was palpable on deep inspiration and also there was a mass in the epigastrium 'running toward' the liver

A barium x ray gastro intestinal examination supported the diagnosis of carcinoma of the pylorus Gastric analyses showed no free hydrochloric or lactic acid and no blood but fat and starch were present In the fractional test the total acidity ran 38, 28 40 33, 40 37 with never any free acid No occult blood was found in the feces Erythrocytes 1 200 000 hemoglobin, 3.6 gm leukocytes 10 300, polys, 76 per cent, lymphos, 24 The Wassermann test was negative The urine examinations and blood chemistry were approximately normal

The patient failed to improve and died on October 26th of pulmonary edema and exhaustion The clinical diagnosis was carcinoma of the stomach and chronic myocardial exhaustion

*Autopsy* (17 606 Dr Weiss) —The stomach near the pylorus shows this considerable mass which is hard nodular, and ulcerated and with raised everted edges obviously a carcinoma The pylorus is constricted (5.5 cm in circumference), the rest of the stomach somewhat dilated but free from serious disease

The nearby lymph nodes are diseased. They are enlarged, but discrete somewhat firm and yellowish, and when I cut through one it is seen to contain caseous material. Section through the gastric tumor, on the other hand, shows a relatively firm gray glistening tissue with fibrous tracery and without necrosis. No other metastases of the tumor can be found.

The heart is also of interest in this case. You see a number of irregular yellowish nodules (pinpoint to 3 mm in diameter) scattered over the pericardium. They look like tubercles and were shown to be so by microscopic examination. These can be traced up along the great vessels until in the mediastinum and around the trachea and esophagus there are found a number of greatly enlarged nodes partially fused and adherent to one another and the surrounding tissues. It is easy to picture that they must have pressed considerably upon the trachea and vessels during life. On section you see that they are largely filled with caseous material and likewise tuberculous. The heart itself is much enlarged, weighing 900 gm, but suffers from considerable mitral aortic and tricuspid disease, the first two with calcification. The tuberculosis does not extend into the auricle, as in a similar case that we presented a few weeks ago, but here is limited to the pericardium.

There is also active caseous tuberculosis in both lungs, liver, kidney, and spleen.

DR WEISS: This case came to us with a clinical diagnosis of carcinoma of the stomach with signs of a mass in the abdomen, and confirmatory x ray findings, but also with definite respiratory signs for the last couple of years. Section proved this mass to be an adenocarcinoma, and one wondered whether this case could be carcinoma with metastasis to the pericardium. Dissection proved the mass in the mediastinum to be poorly demarcated but made up of a collection of large lymph nodes. On sectioning these I found the surfaces to be of a grayish black color and containing an abundance of caseous material. The question then arose as to whether we were dealing with a primary tuberculous pericarditis with secondary tuberculosis of the mediastinal lymph nodes or with primary tuberculosis of the mediastinal



lymph nodes extending to the pericardium. This type of tuberculosis has occurred frequently of late in this laboratory and our guess at the autopsy table was the latter.

DR KRUMBHAAR. The interesting thing to me in this case is the combination of active tuberculosis with cancer. This is a relatively rare occurrence and I cannot recall in our six and one half years here a similar example of an active cancer with active tuberculosis. We have had of course many cases of in active or chronic ulcerative tuberculosis associated with cancer, but in this case the tuberculosis was the more active of the two and most of the small nodules about which there is some doubt in the other organs turned out microscopically to be tuberculosis rather than cancer. Even the gastric nodes seem to have been tuberculous rather than neoplastic. Although both factors undoubtedly played a part in the patient's death the tuberculosis was probably the more potent of the two. Perhaps instead of their being antagonistic in this case as some believe the two diseases were cooperative. The hypothetical antagonism between cancer and tubercle is I suppose chiefly based on the infrequency with which they are found active in the same person. The different age incidence has been offered as a possible explanation while others see in the diminution of tuberculosis a possible explanation of the modern increase in cancer incidence. A recent editorial in the *Lancet* (October 16 1926 p 816) discusses this matter in more detail and presents some evidence for an association rather than an antipathy of the two diseases.

AN INTERN. Isn't there usually more metastasis in carcinoma of the stomach?

ANSWER. Yes though not as much in the scirrhus type that this cancer seems to be as in the softer encephaloid cancers. Also we must remember that the tuberculosis may have carried the patient off before the cancer had reached the metastasizing stage. Metastasis usually occurs relatively early to the liver by way of the pyloric group of lymph nodes especially in pyloric carcinoma. Fundus carcinoma on the other hand is apt to spread by way of the cardia or splenic groups. The left supra clavicular node which is said to be characteristic of gastric can-

cer, and sometimes known as Ewald's node, probably becomes infected by way of the thoracic duct. It should be noted that in some cases such an enlargement is found to be inflammatory rather than truly metastatic.

GRADUATE STUDENT: How can you be expected to make a diagnosis of cancer during the operable period of such a case?

ANSWER: You can't, especially where, as in this case, the symptoms and signs were predominantly those of the associated tuberculosis. It is just in gastric cancer, too, that the slogan of the cancer associations of early diagnosis and early operative treatment falls down the hardest, and this is most unfortunate, as gastric carcinoma is the commonest type of cancer in males. It is only too well known to any practitioner of medicine from bitter experience that this form of cancer may occasionally be absolutely "silent" or so misleading in its manifestations that when it first reaches the clinician it is already inoperable. In more cases, however, the patient may come to the physician and his suspicion be aroused in time by vague symptoms (and we must admit that there is no definite symptom complex for early gastric carcinoma) and yet invaluable time is lost in reaching a diagnosis, so that the exploratory operation is carried out too late. One of our best students of cancer in this country, I am told, has periodical barium-x-ray studies made of his stomach on the chance of detecting an early carcinoma. While this is not feasible for the general public, it is certainly true that the more adequately the public is taught to consult physicians early and the sooner doubtful cases are carefully studied and decisive treatment instituted, the higher will be the percentage of cures in these difficult "internal" as well as the "external" forms of cancer.

DR. CARNETT: In addition to Ewald's node in the left supraclavicular region, the nodes in the left axilla may be found involved in late gastric cancer. My attention was called to this latter fact by Mr. David P. D. Wilkie, the celebrated surgeon of Edinburgh, who was recently in this country, and who had confirmed an observation to that effect made to him by an Irish visitor to his clinic. Occasionally subcutaneous nodules in the region of umbilicus due to lymphatic permeation along the round

ligament are also encountered. About a year ago we had a patient on whom we contemplated operating for cancer of the stomach. He had three small subcutaneous nodules near umbilicus which he claimed had been present for eighteen years. We were skeptical and excised one for biopsy. It showed metastatic adenocarcinoma, hence we did not operate on the stomach. At necropsy the peritoneum covering and adjacent to the round ligament was covered with cancerous nodules. Sometimes metastasis to the umbilicus is manifested by a certain fixity or rigidity of the umbilicus in the absence of superficial nodules. Very exceptionally the skin over the umbilicus is reddened as though subacutely inflamed. We also make preoperative rectal examinations in such cases to determine whether there has been any deposition of transplants at the bottom of the pelvis, presumably having reached there by gravity.

The insidious progress of gastric carcinoma is well illustrated in the recent death in this country of a roentgenologist of international reputation. Somewhat below par and returning from a vacation without having recuperated as expected, he underwent a routine physical examination with x-ray study of the gastrointestinal tract. To the astonishment of all concerned, the films revealed an inoperable carcinoma of the stomach which proved fatal after some months. Such an occurrence in a medical center to a leader of his specialty shows the magnitude of the problem that these cases present.

### CARCINOMA OF ILEOCECAL JUNCTION

PRESENTED BY DR. MULHOLLAND

Case II (Dr. Ormond).—The patient F. E. was admitted 10-14-26 with a chief complaint of occasional vomiting since the previous October with abdominal pain. On April 21, 1926, he manifested acute abdominal symptoms and was operated upon at the Pennsylvania Hospital for appendicitis. At operation the peritoneum was found to be studded with small, hard, white nodules and a gross diagnosis of tuberculous peritonitis was made. The cecum was very much indurated. Microscopic

examination of the appendix showed metastatic gelatinous adenocarcinoma of the meso appendix. The primary lesion was not known, but because of the induration of the cecum that site was suspected. The patient did poorly and was discharged five weeks later. He returned with a superficial abscess in the abdominal wall at the site of incision. This was drained and healed. He soon stopped going to the Pennsylvania Hospital Clinic for x ray treatment.

While at home he grew weaker, had edema of the feet and a productive cough. He later developed persistent vomiting and diarrhea.

His past and family history were unimportant.

*Physical Examination*—The patient was much emaciated. No lesions could be found in the lungs. The abdomen was tense throughout but there was no pain or tenderness except in the right flank. There tenderness was extreme and a mass could be distinctly felt. In the most posterior portion of the flank and pointing near the crest of the ilium there was a hot tender fluctuating mass. No signs of fluid were noted within the abdomen.

*Laboratory examinations* showed the urine to be essentially negative. The blood Wassermann test was strongly positive. The sputum was reported positive for tuberculosis on two occasions.

The temperature ranged from 97° to 99.5° F., pulse 100 to 160, respiration 20 to 30.

*Course*—The patient rallied little under stimulation. In spite of the positive sputum report, no signs could be found in the lungs. He showed no signs or symptoms in the chest until near the end when congestion was noted at the bases. He died on October 22d, eight days after admission.

*Clinical Diagnosis*—Metastatic gelatinous adenocarcinoma of the peritoneum, syphilis, abscess of the right flank and pulmonary tuberculosis.

*Autopsy* (17,593, Dr. Crawford)—This case showed a wide spread malignant process for one so young.

The external examination revealed only a marked degree of emaciation and poor musculature. The chest was thin and the

abdomen sunken There was a right rectus scar At the site of the incision for the appendectomy performed in April 1926 an abscess was pointing in the right iliac region

On incision of the skin the subcutaneous and omental fat was practically absent The peritoneal cavity was interspersed with numerous dense adhesions and scattered over it and covering the mesentery and intestine were innumerable small discrete grayish white pearly nodules These nodules as most of you can see vary in size from that of a pinhead to much larger ones which measure probably 4 mm in diameter The peritoneum covering the posterior portion of the anterior abdominal wall is thickened and shows these same thickened and elevated pearly white patches which are firm in consistency The omentum is thickened and studded with the same type of nodules The pleural cavities are interrupted by a few bands of adhesions and the base of the left lung is densely adherent to the diaphragm

Examination of the heart gives us a picture which is wholly in keeping with that of a boy of twenty who has suffered from no chronic cardiac difficulties The heart musculature is pale and flabby no doubt due to the toxicity of the malignancy which also accounts for the marked emaciation found

The left lung is well aerated and shows only at the base contiguous to the adherent pleura an area where the lung feels firmer than normal You can see scattered throughout the left lung many pinhead sized brownish foci that are slightly raised above the surface and well marked off from the surrounding tissue giving a mottled appearance to the lung These are no doubt areas of bronchopneumonia The right lung much resembles the one on the opposite side Both show evidence of congestion and edema The glands at the hilum of the lung are not enlarged or caseated The spleen is closely adherent to the diaphragm and the surrounding peritoneum is pearly white and thickened

The kidneys ureters bladder prostate and testes are normal

In the gastro-intestinal tract we find that the stomach and duodenum and upper part of the ileum appear normal As we approach the ileocecal junction however we see about 6 inches

of the lower portion of the ileum and cecum surrounded by dense adhesions. These are closely matted together and the junction of the two portions of the intestine form a U shaped structure. The process in some areas appears ulcerative and shows marked thickening of the intestinal wall. In the thickened areas the tissue presents a rather tough homogeneous appearance. As one looks at the ulcerative lesions, they appear as rather ragged structures about 0.5 cm. in depth with irregular and firm edges and necrotic bases. The normal external markings of the intestine at the ileocecal junction have been destroyed and as we now cut through the mass we see that the lesion involves the whole thickness of the intestinal wall. The cut surface of the lesion is glistening and shiny white or gray in color. It tends to be rather hard and firm and when scraped across one can see a small amount of gelatinous or colloid material on the edge of the knife. The remainder of the color appears normal. Posterior to the cecum there is a necrotic cavity with ramifying tracts, one of which extends to the surface just above the crest of the ilium. As we trace another one anteriorly we find that it runs to the anterior surface of the ilium. And here still another can be seen running downward and backward to the bodies of the vertebræ. The bodies of several of the vertebræ have been eroded.

The liver is of normal size and weighs 1330 gm. The capsule is thickened in places, but on section the liver substance is rather pale brown in color, but, as you can see on repeated section no lesion can be observed. The liver, gall bladder, and pancreas show no gross lesion.

Summarizing we may make a pathologic diagnosis of emaciation, right rectus incision, abscess of the right flank, toxic myocarditis, adhesive pleuritis, bronchopneumonia, congestion and edema of the lungs, gelatinous adenocarcinoma of the ileocecal junction with metastasis to parietal and visceral peritoneum, perforating abscesses in the region of the ilium, erosion of the vertebræ.

PHYSICIAN: How do you account for the lack of metastasis to the liver?

ANSWER This carcinoma was fairly well localized to the ileocecal region and to the peritoneum. It is evident that its metastases were all of the lymphatic or else of the transplantation type. It is well known that transplantation is rather common in the peritoneal cavity. These that we see on the posterior surface of the anterior abdominal wall and in the substance of the omentum are of this type no doubt. Then with the ulceration present it is easy to see that pieces could be broken off and carried to different parts of the abdomen. I believe that even lymphatic metastases in these cases is a rather late feature and therefore liver metastasis would also be late.

INTERN Why is there so much ulceration?

ANSWER Gelatinous adenocarcinomata as a rule tend to produce large bulky masses much of which undergoes a gelatinous or colloid degeneration. A large portion of the intestine may be involved but stenosis is not common and as I said before lymphatic invasion is late. The tumor ulcerates early and may as we see in this case extend to the peritoneum with numerous gelatinous nodules as a characteristic feature.

PHYSICIAN Do you think the operation lighted up the process and caused it to progress much more quickly?

ANSWER Yes it no doubt did. This man showed none of the secondary results that we see in long standing tumors of the intestine namely dilatation and hypertrophy of the portion of the bowel above the carcinoma. Also we know that at the appendectomy last April no suspicious mass was observed. In cases where the tumor is large we often see chronic or complete obstruction. Ulceration and hemorrhage is often seen. Infectious peritonitis may be experienced in some cases. The perforating abscesses here no doubt contained some organism of low virulence. A culture has been taken but no matter what organism is found we must remember that the malignancy was the primary cause of this man's trouble. We are not able to venture a guess what would have been his term of life had the abdomen not been opened. He would no doubt have finally succumbed to one of the secondary results or perhaps from the toxicity that accompanies all malignancy.

DR KRUMBHAAR I would like to call attention to the absence of ascites in this case, although there was a marked carcinomatosis of the peritoneum Does anyone happen to know if this type of peritoneal cancer is less apt to cause effusion than others? I have seen ascites present in other cases of gelatinous carcinoma and sometimes bloody, but do not know its relative frequency

The discrepancy between the positive sputum report and the absence of tuberculosis in the lungs calls for comment even if it cannot be adequately explained A single positive finding of tubercle bacilli might perhaps be due to a mistake in diagnosis, reporting etc, but it is hardly conceivable that this should happen twice in the same individual's sputum in any well conducted laboratory, unless some persistent error had crept in, such as contaminated slides or water either of which would affect many other reports as well We have frequently had occasion here to note how often repeatedly negative sputum reports were followed by postmortem finding of some chronic non tuberculous lesion, but must concede that a proper positive finding of acid fast bacilli must mean tuberculosis in the vast majority of cases As no evidence of tuberculosis is demonstrable in these lungs we must assume that it is present in some part of the respiratory tract not examined at autopsy It is even more unlikely that we are dealing with some acid fast organism other than the tubercle bacillus or that such lungs as these could furnish tubercle bacilli to the sputum

### CARCINOMA OF LIVER AND GALL BLADDER

PRESENTED BY DR MULHOLLAND

Case III (Dr Ormond)—L H, an adult white male of sixty five years of age was admitted October 26 1926 with a chief complaint of pain and swelling of the abdomen of three months' duration The pains at first only lasted a few minutes, but gradually became more severe and about one month before admission he began to lose his appetite and weight He then noted that the pains were more frequent and that his abdomen began to swell



The family history was negative for tuberculosis diabetes or malignancy

The patient was only an occasional user of alcohol He was always in very good health until the onset of the present illness

Physical examination showed emaciation and jaundice the latter being noted both in the pigmentation of the scleræ and skin Examination of the chest showed an impaired percussion note anteriorly and dullness at both bases which was more marked on the right probably due to fluid and some hypostatic congestion The mitral first sound was blurred the second aortic slightly accentuated The arteries were markedly sclerosed The blood pressure was recorded as 105/60 The abdomen was distended The skin was smooth and shiny the umbilicus was flattened Prominent veins were noted extending from the sternum to the umbilicus The liver was palpable—four fingerbreadths below the costal margin Shifting dullness was noted in both flanks Rectal examination revealed a prostate that was tender enlarged firm and showed many hard nodules

Laboratory & Ray reported no demonstrable involvement of the dorsal or lumbar vertebræ The pelvis and sacrum were apparently normal The urine showed a trace of albumin an occasional leukocyte a few red blood cells and much mucus was noted Blood examination showed 4 500 000 red blood cells 9600 white blood cells 13.1 gm hemoglobin polys 8 per cent lymphocytes 20 per cent transitional cells 2 per cent Blood sugar was 96 mg blood urea 18 mg The abdominal fluid showed 460 cells per cubic centimeter

During his stay in the hospital his temperature ranged from 98° to 99.5° F pulse from 70 to 100 respirations 20 to 30

November 3 1926 the abdomen was tapped and 3 liters of a clear straw colored fluid was removed The liver was then noted to extend to the umbilicus and a preponderant left lobe enlargement which tended to be nodular was found

November 23 1926 3900 cc of a dark clear fluid was removed from the abdomen The patient became progressively worse and died November 26 1926

The final clinical diagnosis then made is given as secondary carcinoma of the liver, primary site unknown arteriosclerosis, and myocardial degeneration

*Autopsy* (17 688, Dr Walsh) —Many pathologic lesions of interest both for the clinician and for the pathologist were found in this case, with a good concordance between the clinical and pathologic findings

Little was evident on external examination except the signs of emaciation and undernourishment. Contrary to the first physical examination the abdomen rather than being distended was scaphoid in type

As we examine the heart, perhaps the most frequent organ to cause generalized anasarca we see a few easily separated adhesive tags. The mitral valve shows a smooth and glistening thickening along its free edges which one could easily imagine as causing a slight stenotic, presystolic murmur with the systolic regurgitation. The cardiac musculature is dark reddish brown and of normal thickness. The aortic valve is slightly sclerosed at its base

The two lungs closely resemble each other, with congested lower lobes dripping a watery and frothy bloody fluid. In the lower portion of the right pleural sac about 250 c c of a bloody fluid was found, thus confirming the clinical observation made a month ago, though, of course, the amounts present may have varied considerably in that time

The spleen, as you see, is about normal in size and weighs 300 gm. The capsule is thickened in many places over the surface. These areas of thickening are grayish white in color and smooth and hyaline like in character. The cut surface is purplish red in color and the whole organ is rather firm

From the clinical data we heard that the kidneys were excreting a urine which varied in specific gravity from 1015 to 1026 and showed a trace of albumin. The blood chemistry, as I remember it, was normal. As we take up the kidneys, we see two organs that vary in size and shape. The left is much smaller than the right. It is firm and hard. The cut surface is normal. The capsule strips with difficulty, being closely adherent in

rather deep crypts over the surface. However, the pelvis is slightly dilated and shows an injected roughened mucous membrane. The right kidney has much the same appearance as the left with the exception that as we section it we see at the upper pole an area measuring 1.5 to 2 cm. in diameter that is yellowish white in color and is filled with purulent material. The pelvis of this kidney is also dilated and shows signs of inflammation. So here we have a pair of kidneys that are arteriosclerotic in character but show no other evidence of a chronic diseased process. On the other hand, the pelvis of both kidneys and the upper pole of the right kidney (abscess) are the sites of a more acute process the cause for which we will see as we examine the lower organs of the urogenital system. As you see the ureters are thickened and dilated and the mucous membrane is congested. The congested bladder is also dilated and as one looks into it there is seen an obstruction at the neck which is evidently due to the enlargement of the lateral lobes of the prostate. The mucous membrane of the bladder is reddened and congested.

At the time the patient was first examined by the intern this gland was reported to be enlarged, tender, firm and nodular. Upon further examination by a genito urinary specialist and by x ray examination malignancy was ruled out. As we now examine it we see a gland that is hard and firm and nodular. When it is cut across one sees that the surface is yellowish white in color and rather uniform in consistency, without the stony like hardness of a malignant gland.

We now come to the salient organ showing the greatest pathologic change and no doubt the cause of death in this case. You will recall that physical examination showed first an abdomen markedly distended with a liver palpable four finger breadths below the costal margin, which after paracentesis was nodular with predominant enlargement of the left lobe. This liver is greatly enlarged, weighing 2850 gm., and over the whole surface one sees raised grayish white nodules. These nodules are rather firm and hard and many of their centers tend to be umbilicated or sunken. The borders of these nodules are rather sharp. They tend to be pushing aside the liver substance rather

than infiltrating between its elements. On section of the left lobe, you see that almost the entire liver substance is replaced by a firm yellowish-white growth. Smaller but similar nodules are seen in the right lobe. Each of the nodules are hard and firm and tend to be rather discrete. None of the nodules seem to be pressing on or infiltrating the portal vein, so that it is probable that the portal stasis was due to the slowing in the blood-stream within the liver rather than from some pressure from without. As we now examine the gall-bladder, we see that the wall is greatly thickened and firmly plastered to the liver. Upon opening the gall-bladder it is found to contain about 20 pale yellowish stones. These are crystalline in character and are made up of cholesterin and bile-pigments. At the fundus of the gall-bladder there is a raised growth with an irregular surface which is hard and firm. When this growth is cut into, it is found to be infiltrating both the gall-bladder and the liver. It is perhaps primary in the liver, extending into the lumen of the gall-bladder, but this point is easily disputable. Is the malignancy present primary in the liver or did it have its beginning in the fundus of the gall-bladder? The fundus of the gall-bladder is the most frequent site of malignancy in this organ and this is the point we find involved in this case. Then, too, we must remember those gall-stones. They may have seemed of little consequence, but when we read statistics that 84 per cent. of all carcinomas of the gall-bladder show cholelithiasis, and that 14 to 18 per cent. of all cases showing gall-stones become malignant, we must give this evidence due weight. Examination of frozen sections from this case, however, show a type of malignancy which is very fibrous and scirrhus in type. This is, of course, what we would expect from the extreme firmness of the growth. The cellular elements appear to be small cylindrical or cuboidal cells that arrange themselves in acini and at times seem to form small dilated ducts. In other cases they arrange themselves in small islands where the cells seem to be more polyhedral in shape and less deeply staining. This picture to me seems to resemble more the type of carcinoma one would expect to see as having its origin from the intrahepatic bile-ducts.

So in summing up this case I would present it as one showing emaciation, arteriosclerosis abdominal ascites, adhesive pericarditis, brown atrophy of the heart muscle, chronic valvulitis over the mitral valve, congestion and edema at the bases of both lungs, slight hydrothorax on the right, chronic perisplenitis, arteriosclerotic kidneys with pyelonephrosis abscess at the upper pole of the right kidney, ureteritis, chronic cystitis, hypertrophy of the prostate cholelithiasis carcinoma of the liver which shows multiple nodules and is infiltrating the gall bladder

PHYSICIAN Is not primary carcinoma of the liver rather rare and how is it manifested?

ANSWER Yes carcinoma of the liver only constitutes about 0.5 per cent of all cancers. It is of three main types (1) There is first the type arising from the liver cells themselves so-called hepatoma. These cells arrange themselves in masses and tend to crowd the other liver tissue aside. (2) Next we have the type arising from the hepatic bile ducts where there is a proliferation of the bile ducts resulting in a malignant cholangioma. (3) Then there is a variety that results from a combination of these two thus bearing on the argument whether the liver cells arise from the bile ducts or the bile ducts come from the liver cells.

On the other hand carcinoma of the gall bladder constitutes about 5 per cent of all cancers. It too may be one of several types of which Ewing classifies three (1) A papillary cauliflower like form which grows out into the lumen of the gall bladder and eventually distends and obliterates the gall bladder and forms a bulky tumor. (2) A gelatinous carcinoma may be found which may fill the gall bladder and early extend to the liver, lymph nodes and peritoneum, histologically resembling gelatinous cancer of the stomach and intestines. (3) The last type of gall bladder carcinoma is the one that would be most apt to be confused with the tumor we find in this case. This is the infiltrating type which begins as a thickening of the gall-bladder wall and may infiltrate the liver and adjacent lymph nodes and run a course chiefly as a secondary liver carcinoma. This last type of tumor is nearly always scirrhous and metastases are frequent. The cellular elements are columnar or cuboidal in

type and arrange themselves in an adenoid form. Thus when we recall the mental picture of a scirrhous adenocarcinoma on the one hand and on the other a carcinoma which is made up of small cuboid cells which arrange themselves in acinous like structures resembling the bile ducts, we see even the microscopic examination may fail in making an absolute diagnosis. The end result is of course chiefly one of classification.

DR KRUMBHAAR. Dr Mulholland has presented the pros and cons of the primary origin of this tumor so well that one can add to it little more than registration of one's opinion. When this autopsy was performed bearing in mind the greater frequency of gall bladder cancer, the associated gall stones, the secondary nature of most of the liver nodules and the general appearance of the primary mass, I felt that the tumor had probably started in the fundus in spite of its relatively small size there and grown by extension into the left lobe of the liver with secondary metastases throughout the liver. Frozen section has ruled out hepatoma but leaves one in doubt between adenocarcinoma of the bile ducts and the gall bladder wall. However it is quite possible that Dr Mulholland's view is correct and I understand that Dr Eiman also favors the primary site in the liver. (N. B.—Later paraffin sections from several areas in the primary mass showed such a tendency to the formation of round duct like structures lined with low cuboidal epithelium that the possible liver bile duct relationship is strengthened though as Ewing points out [Neoplastic Diseases 2d ed. p. 696] this appearance may also be found in very malignant types of gall bladder cancer.) I want also to mention that squamous cell carcinoma is not uncommon in the gall bladder, presumably arising from epithelium originally columnar but which has become squamous by metaplasia.

It is perhaps noteworthy that no carcinoma was found elsewhere in the body. Wide spread metastases are usually considered evidence of great malignancy and in most senses they undoubtedly are, but malignancy is a complex concept and it is equally possible to consider that a high degree of malignancy, say from the point of view of toxemia, may kill the patient

before metastases occur Friability of the tumor structure tendency toward or accidental invasion of lymph or blood stream and similar items must of course be taken into account in attempting to evaluate the malignancy of a given tumor from the point of view of metastases

# CARCINOMA OF THE BREAST WITH METASTASES TO LYMPH NODES SKIN LIVER EPICARDIUM AND BONES

PRESENTED BY DR CLAYTON

Case IV (Dr Gotten) —J W a white woman aged ninety one presents a primary scirrhous adenocarcinoma of the left breast with extensive metastasis Some of the metastatic growths are very interesting but it is difficult to explain by what route they reached their positions

The patient was admitted April 10 1926 complaining of pain in her right hip and a painful tumor in her left breast She claimed that there was never a nipple on her left breast Only a dimple was present and she remembers that her breast was never like other girls

In 1923 she bruised her left breast so severely that it bled and became discolored down as far as the upper part of the abdomen Six months later she noticed for the first time a small hard painless mass in the upper outer quadrant of this breast and six months after that one year after the trauma a slight amount of purulent and bloody discharge was noticed from the nipple region The breast gradually increased in size and continued to bleed occasionally and drained pus Pain was never marked and she described it as aching

In April 1924 she developed pain in the left hip followed shortly by pain in the right The pain was severe but did not radiate She was bedfast since the summer of 1925 because of this pain She has lost a great deal of weight during the past year Her best weight two years ago was 140 pounds her weight on admission was 90 pounds The patient had not had any other complaints worthy of note Her past medical history was negative and there was no family history of cancer

On physical examination the patient was found to be markedly emaciated with a slight amount of edema of the feet and ankles. An ulcerated area the size of a fifty cent piece was present in the upper outer quadrant of the left breast. Its edges were hard and irregular and its surface covered with a grayish crust. Beneath the ulcerated area was a hard, irregular mass attached to the skin and to the muscle beneath, but not fixed to the chest wall. Small hard nodules were present in the skin extending out from the tumor area particularly toward the lower part of the breast, to the upper part of the abdomen, and toward the right breast, which contained larger nodules in its lower half. Several hard skin nodules were also present on the left side of the abdomen, between the umbilicus and pelvis, another on the external edge of the right patella, and two or three about both ankles.

The axillary, supraclavicular and anterior and posterior cervical lymph nodes were enlarged, hard, and fixed. They were the largest on the left side particularly in the left axilla. Both saphenous nodes were enlarged, but not as hard as the other nodes.

The rest of the physical examination did not show anything worthy of note. The Wassermann test was negative, the blood count, blood chemistry, and urine did not show anything of interest other than a slight secondary anemia.

The x-ray examinations showed metastatic growths in the distal third of the clavicles, acromion processes, glenoid cavities, and necks of the scapulæ, also the head of each humerus was involved, especially on the right side. The head and neck of both femurs greater and lesser trochanters, and the proximal fourth of both shafts also showed metastases with doubtful involvement of the proximal portions of both tibiae. There is also involvement of some of the ribs the tenth and eleventh dorsal vertebrae, and probably the twelfth dorsal and first lumbar vertebrae.

The patient continued to become weaker and finally died with signs and symptoms of bronchopneumonia October 24, 1926. The clinical diagnosis was made of carcinoma of the breast, metastases to many bones and terminal bronchopneumonia.



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In April 1924 she developed pain in the left hip followed shortly by pain in the right. The pain was severe but did not radiate. She was bedfast since the summer of 1925 because of this pain. She has lost a great deal of weight during the past year. Her best weight two years ago was 140 pounds, her weight on admission was 90 pounds. The patient had not had any other complaints worthy of note. Her past medical history was negative and there was no family history of cancer.

except the axillary, cervical, and the saphenous glands. The last-named glands, however, did not have the gross appearance of cancer as the others did. The aortic glands at the bifurcation, the common iliac, the external and internal iliac glands also appeared grossly to be carcinomatous.

The glands around the receptaculum chyli were swollen and enlarged, but the receptaculum chyli and the thoracic duct did not show any signs of metastasis.

The liver contained many small metastatic nodules, the largest being the size of a half pea. The spleen, kidneys, adrenals, pancreas, and other organs show no gross metastases.

Microscopic study has revealed the breast tumor to be scirrhous adenocarcinoma, with metastasis to the muscle, pericardium and epicardium, peritoneum, liver and all the lymph-glands and skin nodules mentioned except the saphenous lymph-gland and the nodule over the right patella. The skin nodules around the ankle also are shown to be metastatic carcinomata.

*Comment.*—This case offers many points of interest. In the first place a history of trauma is present. The trauma occurred before a tumor was noticed in the breast. Cancers are preceded by a history of trauma more than any other one thing. Just what changes trauma gives rise to that causes malignancy is unknown, but it does in all probability play a part in the causation of many malignancies, even as in this case when the trauma is of a single occurrence.

Since the tumor was noticed about three years before death and since it rapidly became clinically malignant and has given rise to such an extensive and wide-spread metastasis it, in all probability, began as a malignant tumor. More wide-spread metastasis may be found at autopsy in these breast cancers if the primary lesion and metastasis to vital organs are actively treated with radium and x-ray, and attention is given to the general health of the patient, because life is preserved for a longer period and thus gives an opportunity for distant metastasis to occur by permeation and in other ways. However, a great many cases of longer standing than this one frequently do not show such extensive metastasis.

**A PHYSICIAN** How might it be explained that the metastasis reached the epicardium without involvement of the internal surface of the pericardium?

**DR CARNETT** This probably occurred by lymphatic permeation, which Sampson Handley has shown to be the chief method of extension of breast carcinoma. As there were no growths on the internal surface of the pericardium it is difficult to see how transplantation could explain it.

**DR CLAYTON** It is of interest that the liver did not show more involvement and the other viscera such as the spleen, kidney, and adrenals did not show any. The liver frequently shows more marked metastasis in long standing cases of breast cancer than any other organ. The size and position of the liver and the enormous lymphatic drainage into it will probably explain this frequent extensive metastasis. The absence of marked involvement of the liver and the absence of involvement of the other viscera mentioned in this case and the absence of any growths within the lesser peritoneal cavity support the view that the growths on the peritoneum, mesentery, and omentum are transplants with the retroperitoneal growths arising by permeation from these.

**DR CARNETT** I would rather take the view that the retroperitoneal glands were involved by permeation of lymphatics from the mediastinum and paraortic glands and that this in turn gave rise to permeation extending out to the peritoneal surface. It is possible that some of the peritoneal nodules, however, may be transplants because of their raised character and their being attached by a pedicle. The bone metastases, also, I would think were due to permeation but I cannot take your time now to give the various arguments supporting this view.

In his book on Cancer of the Breast, Handley explains how the cancer cells extend by lymphatic permeation from the breast along the subcutaneous tissues to the epigastric triangle and from thence to the liver. We have evidence of that process in this patient in the way of subcutaneous nodules over the anterior abdomen, nodules in the rectus muscle and in the

anterior parietal peritoneum just below the zyphoid. The greater frequency of metastasis to the liver as compared to other abdominal viscera is due to the liver being situated nearer to the breast and being provided with larger and more direct lymphatic communications with the breast via the epigastric triangle.

In his book and in a recent personal interview Handley maintains that the dominant process by which metastatic breast cancer disseminates in the abdominal cavity is by "transcelomic implantation" and he attaches but minor significance to lymphatic permeation. I believe that the relative importance of these two processes should be reversed.

Handley and I agree that lymphatic permeation is a common process in the liver and that in other parts, especially the deeper or pelvic parts, of the abdomen lymphatic permeation may begin around implanted nodules. I differ from him in my believing that wide spread lymphatic permeation may occur in the abdomen in the absence of implants.

A critical study of the intra abdominal nodules in this patient reveals several interesting points.

(1) The ovaries, Douglas's culdesac, and the deeper pelvis generally are free from all nodules, although this general neighborhood is a favorite site for implantation of cancer cells carried there by gravity from the epigastric triangle or from the superficial surface of the liver. It might be assumed that the recumbent position of this bedfast patient interfered with gravity carrying cancer cells to the deep pelvis, but we have noted similar upper abdominal nodules in the absence of pelvic nodules in patients who had not been confined to bed. The ovaries are favorite sites for metastases in cancer of the breast and the stomach. It has been rather generally conceded that ovarian involvement is due to implants, but some of my recent observations have caused me to suspect they may arise in some instances by permeation rather than by transcelomic implantation. Dr. Clayton has undertaken the microscopic study of lymphatic permeation as it is encountered in the abdomen and I hope he will devote some of his time to the ovarian metastases.

(2) Near the brim of the pelvis several nodules are definitely beneath the peritoneum as can be shown by pushing the peritoneum back and forth over them. They cannot be implants.

(3) In its most characteristic form an implant projects prominently from the peritoneum and has a pedunculated base. There are no such characteristic implants in this case, although I would not wish to be understood as denying that smaller flat nodules with sessile base may be transplants.

(4) The nodules on the parietal peritoneum are all small and flat and give the impression of being under rather than on the serosa. Dr Clayton's microscope will ultimately determine the correctness of this view.

(5) The largest parietal nodule is in the peritoneum of the epigastric notch just below the xiphoid and in close vicinity to a larger nodule in the rectus muscle. These two nodules in conjunction with the subcutaneous nodules confirm Handley's theory of permeation being the process by which cancer cells are carried from the breast into the abdomen. On further investigation we note an unusual finding in this case, namely that the majority of the parietal nodules are located in the upper left anterior lateral and posterior abdomen extending from the large epigastric nodule to the lumbar lymph nodes along the abdominal aorta. I believe these nodules are indicative of lymphatic permeation extending from epigastrium to lumbar nodes but majority of necropsies on breast cancer do not show this chain of nodules. There are no similar nodules in the upper right abdomen.

(6) The shot sized nodules in the fat free mesentery are limited to the mesentery of the jejunum and upper ileum. Each nodule projects equally from the two mesenteric leaflets which suggests that the nodule originated between the leaflets or in the deep part of a leaflet rather than on the surface of either of them. As Dr Clayton pointed out. These become larger toward the mesenteric attachment. I can find only six nodules on the jejunum. They are all situated at the mesenteric border and are smaller than the nodules in the mesentery itself. All

these mesenteric and jejunal nodules lie behind the gastrocolic omentum, transverse colon, and great omentum where they must have been protected from any shower of cancer cells originating from the epigastrium or anterior surface of the liver. Ascitic fluid might carry detached cancer particles into otherwise inaccessible situations, but there was no ascites in this patient. These various observations indicate that permeation beginning at the lumbar lymph-nodes and not transplantation was the cause of these nodules.

(7) The two nodules which were located behind the lower ascending colon and which only came into view when Dr. Clayton separated the normal adhesions between the posterior wall of the colon and parietal peritoneum could not possibly have been deposited in that closed-off area by implantation. These two nodules are similar in size to the majority of nodules and undoubtedly arose by permeation.

(8) Except for the larger epigastric and intrahepatic nodules all other intra-abdominal nodules are fairly uniform in size. Certainly none of them are of such outstanding size as to be regarded as a primary implant with a secondary lymphatic permeation giving rise ultimately to nodules near and far of similar size.

(9) The retroperitoneal chain of lymphatic nodes along the abdominal aorta and its branches surely could not arise directly by implantations.

I realize that my arguments do not prove that permeation predominates over implantation in this case, but the evidence afforded by this and several similar cases is fairly convincing, although it needs microscopic substantiation which I trust Dr. Clayton will be able to furnish within the next few months.

The subcutaneous nodules, proven to be cancer by the microscope, in the region of each ankle is worthy of note, as Handley has never observed any below the middle of the thigh. My sincere apologies for being so long-winded, but Dr. Krum-bhaar should have known better than to open the flood gates!

PRIMARY CARCINOMA OF THE BRONCHUS WITH METASTASIS  
TO THE LIVER AND KIDNEY

PRESENTED BY DR CLAYTON

Case V (Dr Dunn) —T D a white man aged fifty eight was admitted complaining of weakness. He had been a heavy drinker all of his life and for the month before admission had eaten very little but had lived practically entirely on alcohol.

About a year before he noticed a swelling in the region of the liver which enlarged somewhat since it was first noticed. The patient had had some bleeding occasionally from the rectum for two months but no other gastro-intestinal complaints. He had had a cough for the past two or three months which recently had become productive of a purulent material. There had not been any hemoptysis. As the history was given by the patient's wife and daughter a more detailed and accurate history could not be obtained.

Family and past medical history negative.

*Physical examination* revealed a white man, fifty three years old in a very weakened condition and having skin lesions simulating pellagra. He was emaciated and comatose.

There was some impairment to percussion at the left base of the chest and the breath sounds were very distant. No other chest signs are mentioned.

There was a diastolic murmur heard over the aortic valve and transmitted to the axilla. The abdomen was flaccid and thin walled. A hard regular and smooth mass was felt in the region of the liver more toward the left lobe than the right. The mass was not movable but descended somewhat on deep inspiration. It was not tender. Spleen and kidneys were not palpable.

Rectal examination showed a tender nodule the size of a thumb nail, just inside of the external sphincter and on the posterior wall. It was firm to hard and bled somewhat on examination.

Blood counts and the blood chemistry were negative. The Wassermann test was positive (two plus). Four days after admission the patient's lungs were full of râles and he was still comatose.

Nine days after admission he was much weaker and had a profuse expectoration of thick tenacious grayish black sputum, but not of a foul odor

x Ray study aside from two small irregular dense shadows in the lower portion of the upper lobe of the left lung revealed no demonstrable pulmonary lesion

"The stomach shows considerable six hour retention at the cardiac end in twenty four hours Contour of lesser curvature suggests extrinsic mass such as a large liver Patient probably has a carcinoma of the stomach with metastasis to the liver

The patient's coma continued to deepen and he died fifteen days after admission A clinical diagnosis was made of carcinoma of the rectum or stomach with metastasis to the liver, aortic regurgitation, arteriosclerosis, lues, hemorrhoids

*Autopsy* (17,693, Dr Clayton twenty four hours after death) revealed a markedly emaciated white man, weighing only 80 pounds There was no adenopathy in the neck, axilla, inguinal region, or elsewhere Rectal examination revealed some induration on the posterior wall between the sphincters, resembling fibrosed hemorrhoids The prostate was negative

On internal examination marked dense pleural adhesions were found over the whole surface of the right lung The left lung was free except for dense adhesions to the diaphragm No mediastinal glands were found enlarged The abdominal cavity was negative, except for a large mass involving the left lobe of the liver

The heart showed thickened and deformed aortic valve leaflets which apparently has caused some stenosis and regurgitation

The right lung, which weighed 960 gm, is markedly fibrotic and anthracotic The whole lower lobe is the seat of an extensive bronchopneumonia At the hila, particularly those of the middle and lower lobes, is a large fibrous area of the diameter of a fifty-cent piece, with bronchiectasis in the center, particularly invading the middle lobe Notice also the purulent bronchitis

The left lung, which weighs 510 gm, is collapsed, and the lower lobe, which is bloody and friable, had to be cut away from



the diaphragm. A small mass can be felt at the hilum. The large bronchus to the upper lobe about 1 inch from its origin contains a hard granular white mass encircling the wall and obliterating at least one half of the lumen. The growth which is obviously a carcinoma extends 2 cm up the lumen of the bronchus and apparently has extended outside the bronchus as a circumscribed mass the size of a ten cent piece and of the same gross appearance as the bronchial tumor. Deeper in the lung tissue just beyond this mass is a cavity the size of a five cent piece containing thick greenish pus and is surrounded by gangrenous lung tissue. Bronchiectasis exists in several areas near the growth. You can also see several small areas in the upper lobe of the lung which appears to be metastatic growths.

The lymphatic glands at the hilum are not enlarged as one would expect. The largest gland found is the size of a pea and full of anthracosis. No other glands in the chest were found to be enlarged and there was no involvement of the diaphragm.

The spleen shows nothing of interest. In the cortex of the left kidney are two firm white small nodules simulating the growth in the lung. The right kidney shows no evidence of metastasis.

The liver which weighed 1850 gm is approximately normal except for this irregular white mass showing through the under surface of the left lobe. The pancreas is adherent to it but not infiltrated. The duodenum is adherent to the right edge of this mass and is infiltrated by it down to the mucosa but the infiltration does not extend through the mucosa. On section through the liver and growth a great deal of milky fluid escaped from the center of the growth (liquefaction necrosis). The mass is the size of one's palm and is fairly well circumscribed. The center of growth is white and fluffy in character and harder toward the periphery. The rest of the liver shows no tumor masses and the gall bladder is uninvolved.

The pancreas is negative grossly. The duodenum is attached to the growth as mentioned above. The stomach and the rest of the gastro-intestinal tract show no gross lesions.

The rectum shows old fibrosed hemorrhoids. The bladder and prostate are grossly negative.

One lymph-gland, the size of the end of one's little finger, was removed from the lesser curvature of the stomach.

Microscopic study has revealed a prickle-cell carcinoma primary in the bronchus to the upper lobe of the left lung and metastatic carcinoma within this lung. Sections from the liver and left kidney showed metastatic growths of the same prickle-cell carcinoma.

*Comment.*—In this case the large single tumor in the liver might have been mistaken for a primary liver tumor had the lungs not been carefully examined. Even after the tumor in the bronchus was discovered, it was difficult to convince several students who were observing the autopsy that the small growth in the bronchus was primary and the very large growth in the liver secondary. The absence of involvement of the glands at the hilum of the lung and the presence of such a large metastatic growth in the liver is indeed difficult to explain. The clinicians in this case made a diagnosis of carcinoma of the liver, and because of absence of respiratory complaints and the presence of the fibrosed hemorrhoids and x-ray study, they felt the liver cancer was metastatic either from a primary growth in the stomach or rectum. Unfortunately the patient's comatose condition did not permit a thorough study. x-Ray of the chest failed to help them.

DR. KRUMBHAR: It might be of interest to mention the fact that apparently there is a real increase in the frequency of primary carcinoma of the lung. Granted that increased attention has augmented the number of reported cases and increased the number of carcinomata previously reported as endothelioma of the pleura or other conditions, nevertheless the impression of most pathologists is probably correct that they do now occur more frequently. Ewing considers that they constitute about 1 per cent. of all cancers and Kaufmann places the figure almost twice as high (1.83 per cent.). Primary lung tumors may arise either from the bronchial epithelium, as in this case, or from the bronchial mucous glands or the alveolar epithelium, though often

in advanced cases it is impossible to make any such distinction. The first of these is histologically either a columnar or a squamous cell carcinoma, the second an adeno- or alveolar carcinoma while the third and rarest varies in structure from cuboidal or flat cells filling the air vesicles to papilliferous cylindrical cell carcinoma.

**GRADUATE STUDENT** How can a prickle-cell carcinoma arise from the bronchus?

**DR LEMAN** This must be explained as a result of metaplasia of the stratified columnar epithelium normally lining the bronchus in this area into squamous epithelium. This is not an infrequent occurrence.

**A PHYSICIAN** Why did not the patient have more and earlier pulmonary symptoms as he had noticed this mass in the liver a year ago?

**ANSWER** This cannot be satisfactorily explained except perhaps on the ground of an inaccurate history. The history as you will remember was given by his wife and daughter as the patient was comatose from his admission.

## **HYPERNEPHROMA OF RIGHT KIDNEY WITH METASTASES TO THE LUNGS**

**PRESENTED BY DR. KRUMBHAAR**

**Case VI (Dr Ormond)**—H F, a white man aged seventy presented an obscure condition which though adequately studied during his two weeks in the hospital did not permit of a correct diagnosis until the autopsy was performed.

He was admitted complaining of a sharp pain in the back of his neck for over a month which seemed to be brought on by any slight jar or movement of the head and radiated down to the shoulders and upward behind the ears and often to the top of the head. The pain began suddenly and often was worse at night. For a week he had had some pain on swallowing and also some pain in his knees.

Two months before admission he had had a twelve hour retention of urine and was treated at home with hot packs and

catheterized, after which he passed several blood clots. He has had no distress or retention since then and was told that he had a possible stricture or tumor. His urine is usually a dark amber and often cloudy.

He had had rheumatic fever thirty years ago, also gonorrhea.

On physical examination he was found to be considerably emaciated with marked pulsations in the neck and the trachea, moving with each systole. There was dullness on percussion below the left clavicle merging with the aortic dullness and also an area between the scapulæ. A few fine rales were heard which disappeared after coughing. His heart was greatly enlarged to the left and downward, with widened aortic dullness. There was an apical systolic murmur and a rate of forty five (45). Blood pressure 130/82. His abdomen was scaphoid, but no abdominal masses were felt, neither were the kidneys or spleen. He had a marked edema of the legs and increased reflexes on the right with a positive Babinski sign. Rectal examination showed an irregularly enlarged prostate, moderately firm and tender.

Laboratory studies gave a negative urine report, hemoglobin 12.1 gm., red blood-cells 3,680,000, leukocytes 9200, polys 76 per cent, lymphocytes 12, large and transitionals 12. The Wassermann blood test negative. The electrocardiogram revealed a 2:1 heart block, thus explaining the slow heart rate.

x-Ray examination revealed "two large circumscribed shadows in the inner portion of the right lower lobe—lymphosarcoma (?) "

After rallying slightly, the patient grew gradually weaker till death occurred fourteen (14) days after admission.

The clinical diagnosis was made of undiagnosed tumors in the chest, enlarged prostate, mitral insufficiency with partial heart block, and generalized arteriosclerosis.

*At Autopsy* (17621)—Dr. Walsh confirmed all of these findings except that, as you see, the prostate is not enlarged. The heart shows thickening of both mitral and aortic valves, calcification of the coronary vessels, and a calcified plaque on the upper portion of the septum, which can easily account for the partial heart block. In addition there was a generalized myocardial fibrosis.

The most interesting lesion is in this large (450 gm) right kidney, where almost the entire kidney substance (except for a small bit of the lower pole) is replaced by a yellowish mass that is obviously a neoplasm. It is firm and hard with a glassy cut surface dotted with hemorrhagic spots and small regenerative cysts. The renal vein is dilated with yellowish cheesy material. Two small masses 6 cm long below the kidney and attached to the vena cava contain the same material and are apparently obliterated tributaries. When the capsule is stripped further it tears the tumor substance to which it is firmly adherent but many smaller nodules are visible through it. As microscopic examination has since confirmed this was correctly diagnosed by Dr. Walsh as a hypernephroma (see Comment). It is of the type with large masses of cells without foamy protoplasm and containing a moderate amount of fibrous tissue. The other kidney which shows some diffuse nephritis and the adrenals show no gross evidence of disease.

In both lungs however you see many small hard circumscribed nodules scattered through the lung tissue which are firm and pearly white throughout on section and not surrounded by any inflammatory area. The chronically thickened pleura prevents the inspection of these nodules on the exterior. These lungs weighed 500 (left) and 700 gm.

*Comment*—This is an interesting example of how silent a malignant tumor may remain during its curable period eventually to produce misleading symptoms elsewhere. The urinary attack two months before admission now becomes clear but at the time even though it aroused the suspicion of tumor it cleared up so satisfactorily and was followed by such negative urinary findings that it was natural to consider it in an old man of seventy as an accompaniment of the enlargement of the prostate which did not materialize.

The recent and I believe correct tendency with pathologists is to consider fewer of these tumors as coming from adrenal rests and more of them as true renal tumors. Without going into the details of this discussion the absence of the foamy protoplasm and the arrangement of cells would support a renal origin in this

case, even though no lumina or papilli were found. The tendency to invade blood-vessels is characteristic of either form.

A GRADUATE STUDENT: How do you explain the pain in the back of the neck?

ANSWER: This pain, the chief complaint of the patient on admission, not only was misleading at the time, but is still baffling. It is possible that a special postmortem investigation of the neck might have offered a satisfactory answer—a procedure that unless specially requested would be almost a practical impossibility on account of the number of autopsies performed here daily—but with the material and evidence now available it is impossible to offer a satisfactory explanation.

AN INTERN: How about the two shadows in the right lower lobe?

ANSWER: In the absence of any other cause of increased density these must undoubtedly have been caused by the metastatic growths in the lung, though, as you have seen, both lobes are fairly well seeded with small metastases and there are no two large masses in this area. While, therefore, the radiopathologic evidence here cannot be definitely correlated, it may serve as an occasion to emphasize that x-ray pictures merely demonstrate shadows, and that these may be of the most varied and in some cases complicated origin, so that great caution should be exercised in drawing deductions, especially from single exposures. We have found here that x-rays of the lungs on admission of malignant cases are most useful in often establishing the presence of metastases in a given case and thus preventing useless radical treatment. Of greatest importance in this diagnosis is the increase in size of suspicious nodules in a roentgenogram taken a week or two after a suspicious first examination.

## MELANOMA OF CHOROID(?) WITH NUMEROUS METASTASES

PRESENTED BY DR. KRUMHAAER

Case VII (Dr. Corrin).—This patient, A. H., a white man eighty-two years old, was brought to the hospital complaining of weakness in the legs, so marked that he frequently fell. This

began about six weeks before admission, with inability to keep his balance and had been steadily getting worse, so that he has been bed ridden for a few weeks. He also became rather forgetful and had lost 20 to 30 pounds in two months for no apparent reason.

The patient's right eye had been removed for what he said was a cataract operation three years before, since which time he wore a glass eye<sup>1</sup>. He had no other noteworthy illnesses, but always was a heavy drinker.

His mother was said to have died of a tumor of the tongue (type unknown) and a brother of an illness similar to that of the patient. One sister died of tuberculosis.

*Physical examination* revealed a fairly well developed but anemic, emaciated individual in distinctly poor condition. The left eye showed nystagmus in all directions, the pupil was irregular, but reacted to light and accommodation. His arteries were markedly sclerotic, his blood pressure 140/50. Except for an inguinal hernia on the right side, atrophy of the skin and marked wasting of the interossei of both hands, his exterior presented no further abnormalities. His lungs showed a few rales at the bases and his heart was feeble and irregular with a mitral systolic murmur. His reflexes were normal.

*Laboratory Studies*—Urine examinations, blood chemistry, colloidal gold and Wassermann tests (both blood and spinal fluid) were all negative.

*Course*—The patient continued with but little change for three weeks, when he began to weaken rapidly and died in a few days.

A clinical diagnosis was made of senility, generalized arteriosclerosis, myocardial degeneration with auricular fibrillation, progressive muscular atrophy, terminal passive congestion and bronchopneumonia.

*Autopsy* (17,651, Dr Walsh)—As soon as the body was opened, it was obvious that the case was one of extensive mela-

<sup>1</sup>It has subsequently been learned that this operation was performed at the Methodist Hospital November 20 1923 for staphyloma and that the pathologic report was sarcoma.

nomatosis Among pleural adhesions on the left side, were several bluish nodules and a larger one at the junction of clavicle, first rib, and sternum A similar mass was noted on the posterior wall of the pelvis

Over the entire surface of this heart you will notice small greenish blue elevated nodules, or others in which melanin is absent, which are yellowish white The same masses, but smaller, are present over the endocardium (especially in the left ventricle), but none in the myocardium, which only shows some whitish streaks on tangential section The muscle is hypertrophied (weight 450 gm) and pale brown and there is sclerosis and calcification of the mitral and aortic valves

The lungs likewise contain many similar firm oval nodules, mostly of the pale variety and thus easily distinguishable from the rather considerable anthracosis The metastases are especially numerous in the right lung, both on the exterior and throughout its substance There are patches of bronchopneumonia in the lower right lobe They weigh 600 and 440 gm

While the fat and connective tissue about the kidney show numerous small black nodules (metastases), you can find none in the substance of the kidney Both kidneys are the seat of moderate diffuse nephritis of the arteriosclerotic type, with small retention cysts

Throughout the liver many of these same greenish blue or yellowish nodules are plainly visible to all They vary considerably in size and bulge above the surface The liver, which weighs 1500 gm, is otherwise normal The gall bladder too has many similar nodules attached to its wall

The gastro-intestinal tract and glands of internal secretion seem to have been spared The bladder is hypertrophied, though the prostate is only slightly enlarged, and is acutely inflamed with necrosis and ulceration of the fundus and an abscess containing thin yellowish pus This skull cap shows many black nodules both in the connective tissue and bone substance One of these is so soft that a probe can easily be passed through

In the light of these findings and the prominent nervous symptoms you will be surprised to see that the brain and cord



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<sup>1</sup>It has subsequently been learned that this operation was performed at the Methodist Hospital November 20 1923 for staphyloma and that the pathologic report was sarcoma.

ANSWER You would certainly think so, and yet cases with the primary site properly authenticated have been known to go even ten or twelve years after its enucleation and obliteration and yet finally succumb with wide-spread metastases

The great malignancy of these tumors when they have once started raises the question as to how to treat their forerunners, the pigmented naevi or moles. The clinician or pathologist having seen the metastatic disaster in full blast is apt to view such cases with great distress; whereas the dermatologist, with attention focussed on thousands of pigmented moles that continue harmless through life, realizes the very small percentage that undergo malignant change. The proper answer seems to be not to excise all such moles as soon as found, but to warn their owners of their potential danger, especially if subject to repeated irritation, and to insist on complete excision or obliteration as soon as they show signs of sudden growth or ulceration. I saw a case recently at the Bryn Mawr Hospital where a healthy iceman noticed that a large mole on his back had broken down, yet failed to have it treated. Within three months he was bed-ridden with extensive visceral metastases and died a few weeks later. In this case not only was the man's urine almost black, but his skin was a dark ashen gray black from the diffusion of the melanin throughout his body.

A PHYSICIAN What caused the central nervous symptoms?

ANSWER In the absence of melanotic involvement of the brain and cord these are probably best explained as due to the cerebral arteriosclerosis and atrophy. Time has not yet permitted sufficient study of the central nervous system to determine whether or not the lesions of true progressive muscular atrophy were present.

*Frederic L. Marshall.*



## CLINIC OF DR J L GOFORTH

FROM THE RADIOLOGIC CLINIC AND LABORATORY OF MORBID  
ANATOMY OF THE PHILADELPHIA GENERAL HOSPITAL

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### GIANT-CELL TUMOR OF BONE

THE central bone lesions comprise a group of neoplasms that possess rather specific features. When all of the aids to bone tumor diagnosis are employed these characteristics, in the majority of instances differentiate clearly between the various types of lesions. The so called giant cell tumor of bone, often referred to as 'giant cell sarcoma', 'myeloid sarcoma' and "osteoclastoma" is the commonest and perhaps the most interesting to surgeons and pathologists, of the central bone neoplasms. That this tumor should be occasionally incorrectly diagnosed and consequently mistreated is due we believe to the fact that hastily formed opinions, based on incomplete diagnostic data, rather than unfamiliarity with its general clinical, roentgenologic, and pathologic characteristics, serve as guides to treatment procedure. It is admitted that our knowledge and interpretation of the etiology, behavior and course, and histogenesis of the tumors of the giant cell series is very incomplete, but, as with electricity even though we do not thoroughly understand the tumor we can successfully deal with it. It is the purpose of this paper to outline the features of giant-cell tumor, and to evaluate them as aids to diagnosis. Information obtained from all possible sources establishes an integrated diagnosis which is the proper guide to treatment procedure, and which in the end, becomes our only true measure of tumor behavior.

**Etiology**—Trauma is often mentioned as a possible cause of giant cell tumor. Patients frequently date the onset of symp-

toms with some form of injury such as a bruise resulting from a fall. When it is recalled that the majority of tumors when first seen are well formed structures and that the neoplasm is essentially a relatively slowly growing tissue the time of origin becomes a factor which is practically immeasurable. It would appear then that trauma is a result of, rather than a cause of, the growth and the usual history of injury may be regarded as evidence that the tumor had weakened the involved bone to the point of unreliable support at the time of the injury.

Opinion is divided regarding the nature of a giant cell tumor. Barrie<sup>1</sup>, Meyerding<sup>2</sup> and others regard it as being primarily a local chronic inflammatory process. Ewing<sup>3</sup> and Bloodgood<sup>4</sup> consider it a special type of vascular granulation tissue tumor. Stewart<sup>5</sup>, Finch and Gleave<sup>6</sup> and others believe that it is a true neoplasm. In a previous contribution<sup>7</sup> evidence showing that the giant cell tumor possesses several features common to neoplasms and that in rare instances it may actually metastasize was adduced.

It has been suggested that an etiologic and developmental relationship exists between bone-cysts, the different stages of osteitis fibrosa and giant cell tumor. Martland<sup>8</sup> regards giant cell tumor as a phase of osteitis fibrosa cystica. Whether or not these entities are stages of the same general process will depend on the establishing of the exact mode of origin and life history of each of the central bone lesions. The evidence at present we feel warrants giant cell tumor being classified as a true tumor.

**Occurrence and Location**—Giant cell tumor occurs characteristically in the epiphyses of the long bones of young adults. Both sexes are affected but the majority of cases reported have been in females. 27 of the 50 cases studied by Coley<sup>9</sup> occurred in females. A high percentage of cases are seen between the ages of twenty and thirty five; a few instances have been reported in individuals below ten and above fifty; however, the head of the tibia and fibula, lower end of the femur and the lower ends of the radius and ulna are especially favorite sites for giant cell tumor. Less frequently the humerus, os calcis, ilium, clavicle and the phalanges are elected. In one of our cases the growth

was located in the trochanter and neck of the right femur, and in another recently studied the entire lower end of the humerus was involved. Although the tumor is practically always solitary, there are a few cases on record in which it appeared in multiple form.

Giant cell tumor may be confused with the benign bone-cyst forms at times. According to Bloodgood,<sup>10</sup> bone cysts occur, as a rule, in the shafts of the long bones, and may be multiple. They are most frequently found between the ages of five and fifteen, are first noticed as local swellings without pain, are prone to fracture and are of long duration. His studies would seem to indicate that there is a definite relationship between bone-cysts, osteitis fibrosa cystica, and solid osteitis fibrosa.

**Symptoms and Signs**—Pain and swelling are practically always the initial symptoms of giant-cell tumor. Very slight local pain, often disregarded, is present when the affected bone is bearing weight or is under strain. When attention is thus called to the involved area slight swelling is usually found to be present, and there may be mild tenderness on palpation. Occasionally a fall with attendant injury first directs attention to the affected area, but on questioning the patient a history of pain prior to the accident can be frequently elicited.

As the disease progresses, disability becomes the chief complaint. It is this symptom which most frequently brings the patient to the physician. In each of our cases a definite history of pain, swelling, or injury was found to have preceded disturbance and loss of function three to eighteen months before the patient finally sought medical advice.

Pathologic fracture occurs but rarely in giant cell tumor. The proximity of the tumor to a joint in the majority of cases serves as a protection to the affected bone, and the growth itself breaks through the limiting osteomembranous shell only in late and neglected instances of totally destroyed epiphyses. It is interesting that union may follow fracture.

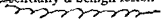
**Physical Findings**—But little positive information may be obtained from the physical examination. The local condition may show nothing beyond slight swelling, tenderness on pressure,

and disturbance of function thus depending largely on the location of the tumor. Secondary manifestations such as edema of an extremity may be present. The laboratory examinations are important in ruling out other lesions. The Wassermann reaction should be routinely performed in all instances of suspected bone-tumors and in urinalysis the tests for Bence Jones protein are of importance in differentiating the condition from primary bone-marrow lesions.

**Roentgenology**—x Ray study is probably the most useful and important aid to bone tumor diagnosis. Moderately advanced giant cell tumor gives such a strikingly characteristic picture that this examination alone often establishes the diagnosis. Typically the lesion is seen as a rounded circumscribed mottled area of diminished density which is bordered by a thin usually intact bony shell (Fig 168). Often the mottling gives a coalescing multicystic appearance to the lesion (Fig 165). The x ray shadows define well the bone absorption activity of the growth—giant cell tumor is not a bone-forming neoplasm. In earlier cases where only an area of fine mottling is visible differentiation from a local inflammatory lesion may be difficult. In advanced cases where fracture or extension of the tumor through its limiting capsule has occurred and in an attempt to effect union irregular bone tissue proliferation is evident it may be impossible to distinguish definitely the condition from osteogenic sarcoma.

x Ray study of the chest and entire osseous system is indicated whenever bone neoplasm is suspected. Multiple lesions can be detected through this procedure only in many cases and differentiation from bone-cysts the various forms of osteogenic sarcoma secondary carcinoma primary bone-marrow lesions tuberculosis and syphilis may depend largely upon x ray study of all bones. We wish to emphasize that x ray examination should be routine and complete in any case where history and symptoms point to possible joint and bone-lesions (See Case II).

**Treatment**—The many contributions on giant cell tumor have shown that it is essentially a benign lesion. Such a verdict



warrants conservative treatment. It must be remembered, however, that the tumor exhibits varying degrees of local aggressiveness in the average case and that under certain conditions, it possesses malignant potentialities. Atypical behavior has been excited under the stimulus of repeated curettage, superimposed infection, and irradiation.

There are four methods of eradicating giant cell tumor—by curettage, resection, amputation, and irradiation. Thorough curettage in conjunction with chemical cauterization is perhaps the method of choice in those cases where destruction is not excessive and where more radical procedure would disturb or destroy function. Lesions in the head of the tibia, upper and lower end of the femur, and lower end of the radius lend themselves well to such treatment in many instances. Tumors of the upper end of the fibula and lower end of the ulna can often be best removed by resection, without resulting disturbance of function. Rarely, when a tumor has destroyed practically all of the epiphysis of a major bone, amputation may be the treatment of choice. Curettage in such instances necessitates long confinement in order for regeneration to occur, and the involved loss of time may be incompatible with the patient's economic status. Treatment of lesions in atypical locations should have as its objective thorough removal of the growth with the least possible anatomic mutilation.

The Roentgen ray and radium have proved of some value in the treatment of giant cell tumor and are employed in several clinics. Ewing<sup>3</sup> advises irradiation without operative intervention on the strength of observations made at the Memorial Hospital. Such treatment unfortunately, does not permit of a confirmatory pathologic study and diagnosis of the tumor, precludes the establishing of definite prognosis, and may leave the physician in doubt in the end, as to what he has actually treated. With our present knowledge of giant cell tumor we feel that conservative, but complete surgical removal of the growth offers the patient the best chance for the earliest absolute cure.

Exploratory incision is seldom necessary, but in those instances where diagnosis is uncertain, and treatment procedure



has not been decided upon it is justifiable. Facilities for establishing immediate diagnosis (frozen section) should be available in such cases and treatment should be guided accordingly.

**Pathology**—Gross<sup>11</sup> classically described giant cell tumor as a spherical growth enclosed in an osteomembranous capsule usually occurring in the spongy substance of the epiphysis red to maroon in color and of spongy and jelly like consistency, resembling exuberant vascular granulation tissue and containing no vestige of the original bone (Fig 169). But little can be added to this. The bony capsule usually conspicuous in x ray study often encloses the entire growth and is composed of flat plaques of bone. Within this shell a layer of dense fibrous tissue varying in thickness is seen. This tissue grossly and microscopically resembles the picture of osteitis fibrosa. The tumor proper may be solid or multicystic. Areas of degeneration may be present.

Histologically the picture of giant cell tumor is specific. Giant cells of the epulis type or osteoclasts varying greatly in number in different cases are seen more or less uniformly embedded in a stroma composed of fibroblastic tissue (Figs 167-171). These giant cells vary considerably in size and contain usually from 10 to 60 small ovoid centrally placed nuclei (Fig 170). The cytoplasm is glassy or opaque acidophile and abundant. We regard these giant cells as being essentially innocent but by reason of their function in bone absorption and their probable origin by fusion of liberated and modified osteoblasts or bone-forming cells they are considered as specific neoplastic cells.

The stroma is composed of loose supporting fibrous reticulum and fibroblastic cells ranging from immature fat spindle cell forms to the adult fibroblast types (Fig 171). We feel that the behavior of this element of giant cell tumor virtually governs the course of the neoplasm. Microscopic study of the cellularity, cell type and cell activity of the stroma offers a fairly reliable criterion of the innocence or local aggressiveness of the tumor and is we believe the most valuable guide to prognosis.

Interest in any case of bone neoplasm should not end with diagnosis and treatment. Occasionally particularly following incomplete curettage or inadequate removal of a giant cell tumor a local recurrence will manifest itself. Such recurrences, although usually essentially benign in character are more virulent, locally aggressive and rapidly growing as a rule than was the original growth. Histologically the stromas of recurrent tumors when compared with sections of the original growth are found to be more cellular and active in appearance. In order that a patient may be given the obvious advantage of the earliest treatment of a local recurrence and that further data regarding the nature and course of giant cell tumor can be obtained a rigid and frequent 'follow up' of every case is imperative. Our knowledge of the true character of giant cell tumor will increase only as further information is gathered from the free use of all aids to tumor study.

#### ILLUSTRATIVE CASES\*

**Case I**—C H white male age thirty two first noticed pain deep in the thigh about 4 inches below the right hip when weight was borne on the right leg. No history of injury. The condition became only slightly worse but, because of persistent pain he entered the hospital at the end of six months. There had been practically no disturbance of function during this period.

Physical examination revealed slight swelling of the greater trochanteric region on the right side. There was no tenderness, and motion of the thigh was free. The other physical findings were unimportant and the laboratory tests were negative. x Ray study showed a rarefaction of the neck and trochanter of the femur, surrounded by a narrow rim of bone, everywhere intact (Fig 164). Based on the history, symptoms, physical findings and x ray study, a diagnosis of "central sarcoma" was

\*These typical cases of giant cell tumor are reported in detail in the December 1926 issue of the Archives of Surgery. They are used here because they illustrate well the features of this specific neoplasm. I am grateful to Dr J B Carnett for permission to use the clinical data in each case.

made and in March 1923 the tumor was removed by thorough curetment by Dr J B Carnett. Convalescence was uneventful; regeneration of bone to the extent of normal density occurred within eight months and when followed up in November 1926 the patient was well without signs of recurrence and was actively engaged in business as a traveling salesman.



Fig 164—Case I. x Ray of pelvis showing a neoplasm occupying the neck and trochanter of the right femur. A narrow rim of bone surrounds the area of diminished density. The growth was removed by curetment, and there has been no recurrence in three and a half years.

*Pathology*—The curettings consisted of small chunks of reddish firm friable tissue intermingled with blood clot. Bone elements were not present. Microscopically great numbers of giant cells of the epulis type or osteoclasts were diffusely embedded in a dense stroma composed of loose fibrous reticulum and mature fibroblasts. There was no evidence of unusual behavior, cell activity or malignancy. The picture was characteristic of benign giant cell tumor.

Case II.—N. P., white female, age twenty-five, entered the hospital complaining of pain and swelling in the right knee, and inability to walk without crutches. Eighteen months previously she had first noticed pain in the knee when standing. There

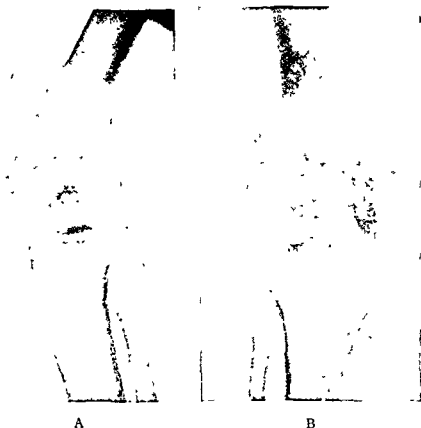


Fig. 165.—Case II. A, Lateral x-ray of right knee. B, Anteroposterior x-ray of right knee showing a neoplasm growing in the epiphysis of the femur. The rounded, mottled area of rarefaction, bordered by a narrow bony shell in places, forms a picture suggestive of multiple coalescing cysts, but characteristic of giant-cell tumor. Note that only the periosteum limits the growth on the fibular side.

was no history of injury. The condition had gradually grown worse, and the knee had become slightly swollen. For four months she had been obliged to use crutches. *Because of a vaginal discharge, which proved to be of non-specific type, the condition had been regarded as a gonorrheal arthritis in three*

Case III —E G, white female, age twenty three, stated that in January, 1926 while walking she had turned her right ankle, and had fallen. One month later she noticed dull pain in the right knee, laterally, which was excited by pressure, or when weight was borne on the right leg. The condition gradually



Fig 168 —Case III x Ray of right knee showing a neoplasm occupying the head of the fibula. The expanded rarefied well circumscribed area forms a picture characteristic of giant cell tumor.

grew worse, and slight swelling developed in another month. The knee often "gave way" when walking. In April 1926 she came to the hospital complaining of pain and a weak knee.

Physical examination revealed definite fulness and tenderness, laterally, immediately below the knee. Function was not greatly

disturbed. The remaining physical findings were unessential. The laboratory examinations were negative. *x*-Ray study showed an expanded, rarefied, well-circumscribed area involving all of the head of the fibula. The picture was typical of giant-cell tumor (Fig 168).

On April 22, 1926 Dr. J. B. Carnett resected the upper 3 inches of the fibula, removing the tumor intact. The patient was discharged from the hospital May 10th, and when seen in

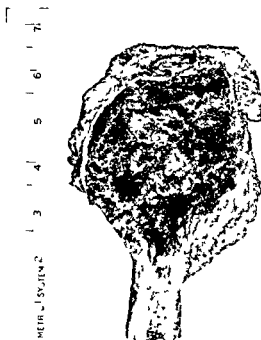


Fig 169 —Case III. Section through a giant-cell tumor of the head of the fibula, treated by resection. Note the ballooned out, osteoperiosteal sac, filled with chunks of friable, bone-free tumor tissue. The limiting wall is everywhere intact. A bony shell is seen circumscribing the growth in places.

November, 1926 was in excellent health, and without signs of recurrence or impairment of function.

*Pathology*—The head of the fibula was replaced by a solid cellular tumor which, on section, was seen as a ballooned-out osteomembranous sac filled with reddish-purple, friable tissue resembling hyperplastic bone-marrow (Fig 169).



# CLINIC OF DRS CHARLES C NORRIS AND M E VOGT

PHILADELPHIA GENERAL HOSPITAL

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## RADIATION IN GYNECOLOGY

BEFORE describing the treatment of various gynecologic conditions encountered in the Philadelphia General Hospital it is pertinent to state that on account of the short space allotted brevity must be emphasized

The following classification is adhered to with such modifications as may seem necessary

Group I —Benign gynecologic lesions

Group II —Malignant gynecologic lesions

Group III —Irradiation dosage

Group IV —Complications encountered

Group V —Autopsy material and findings

Group VI —Rare cases

Group VII.—Photographs and photomicrographs

### GROUP I BENIGN GYNECOLOGIC LESIONS

I Among the benign gynecologic lesions one of the most interesting cases encountered to date and, so far as is known, the only one of its kind treated by irradiation, was a granuloma inguinale occurring in a girl of nineteen. The lesions were of the usual type, moderately diffuse, and involved both labia, the perineum and extended to within 2 cm of the anus. The case was consequently a moderately advanced one. The patient was treated by radium applied by means of a lead plaque. This was moved three times from place to place until the entire area had been treated. The dosage used was 1037 millicurie hours, which is approximately one half the E. F. D. A normal radium reaction occurred with some swelling, inflammation and sloughing of the





leukorrhea in about 75 per cent of the cases, and improvement in the remainder

**Benign Uterine Hemorrhage.**—In properly selected cases myomata and myopathic hemorrhage respond ideally to irradiation. The following contraindication to this form of treatment

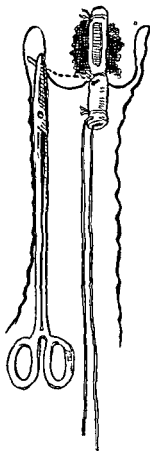


Fig. 172.—Capsule contains radium encased in rubber tube showing method of application in cervical carcinomata. A stitch is passed through the cervix and the suture clamped (Iurness method). The vagina is then packed with dry gauze packing, especial care being taken to keep the bladder and rectum out of the danger zone.

must however be definitely adhered to, although certain exceptions exist

*First* Tumors larger than a three months' pregnancy

*Second* Tumors undergoing degenerative changes such as softening etc

*Third*—Tumors exhibiting rapid growth

*Fourth*—Tumors producing pressure symptoms

*Fifth*—Women under forty years of age except under unusual conditions

*Sixth*—The presence of inflammatory lesions

*Seventh*—Radiophobia

*Eighth*—Other conditions requiring an abdominal section

In other words uncomplicated hemorrhages of benign origin occurring in women over forty years of age are the ideal cases for this form of treatment or in those cases in which operation is contraindicated as in advanced renal or cardiac disease. The advantages of irradiation over operation are the almost entire lack of mortality short hospitalization and the rapidity of convalescence. Bleeding is checked by the treatment in 95 per cent of the cases.

*Technic*—As an accurate diagnosis is essential this treatment should be applied only by one experienced in gynecologic examination. Anesthesia is employed usually nitrous oxid. In case any doubt exists as to the correctness of diagnosis ether anesthesia on account of its greater relaxing properties is preferable. The usual dilatation and curettage is performed and 50 mg of properly screened radium enclosed in a rubber tube of such length so that 1 cm of the tube will project from the cervix when the radium is placed in the fundus of the uterus is inserted into the uterine cavity and held in position by a single stitch. It is essential that the curettings be examined by an experienced gynecologic pathologist in order to exclude the possibility of carcinoma of the fundus being present. If carcinoma should be found a panhysterectomy is indicated. A dosage of 1200 millicurie hours is usually employed. During the period that the radium is in situ a percentage of patients complain more or less of nausea and vomiting. This however is usually not a marked feature and disappears almost routinely with the removal of the radium. The patients are kept in bed for two or three days and are usually discharged in three or four days. Unless radium has been applied just before a menstrual period no subsequent bleeding is likely to occur. If however the

irradiation is given just prior to the onset of a menstrual period, one period is likely to occur. The only unpleasant sequelæ of this form of treatment is that for some months following the irradiation a certain amount of whitish leukorrhea may be noticed. This is easily taken care of, however, by an occasional douche. In cases of irradiation for myomata tumor shrinkage occurs in about three-fourths of the cases, but is usually not appreciable for five or six months. Sterility and the production of the artificial menopause occur. The menopause occurs in about the same percentage of cases, and with about the same severity as would be expected following hysterectomy. In young women profuse hemorrhage of benign origin is not uncommon, and in these cases irradiation has a definite place. Many of these cases are encountered which resist all forms of medical treatment, and the choice must be made between irradiation and operation. Hysterectomy, with conservation of the tubes and ovaries, offers a certain cure. It does, however, definitely sterilize the patient, and even when most carefully performed, is in a small proportion of the cases followed by the neuroses incident to the menopause. On the other hand, if irradiation is employed, the dosage must necessarily be definitely reduced, for if this is not done, permanent sterilization and production of the menopause will certainly occur. It is our custom to explain these facts to the patients and emphasize that the dosage to be employed is a minimal one, and that repetition of the treatment may be necessary. Even if ultimate failure follows irradiation, operation can subsequently be performed. The technic of the operation is the same as previously described except that not more than 300 millicurie hours of irradiation is administered. If necessary the treatment may be repeated in three months. About 50 per cent. of such cases which have been treated by us have been cured, and 30 per cent. benefited. A number of cases of pregnancy following the treatment have occurred in our series. The general postmenstrual history in these cases is that a period of amenorrhea takes place varying from two to three months with ultimate reappearance of the normal flow. We have had 1 case in a girl twenty years of age

who had no cessation of symptoms after the first irradiation and no result from a second treatment three months later. With considerable hesitation a third dosage of 500 millicurie hours was applied. At the present writing all pathologic hemorrhage has ceased and the patient is menstruating normally. This patient was very anxious to have children but pregnancy has not occurred. We have another patient, an unmarried girl of twenty one years of age who had excessive hemorrhage of the menorrhagic type. This patient has had four treatments in the last three years. Each treatment is effective for from three to seven months when a recurrence takes place. After the first treatment no curettage has been necessary and the radium has been applied without anesthesia. Hospitalization is two days, the patient's general health is good and barring the inconvenience of the occasional treatments she is well.

It is probable that irradiation acts in these cases by destroying or inhibiting the development of the follicle bearing portions of the ovary and to a lesser extent by the production of endarteritis in the uterus.

## GROUP II. MALIGNANT GYNECOLOGIC LESIONS

These constitute by far the largest proportion of the cases applying to the Radiologic Department of the Philadelphia General Hospital.

**External Genitalia**—Carcinoma of the urethra is a comparatively rare form of neoplasm and yields poor results following attempts at radical removal by surgery. The majority of cases applying to our clinic have been advanced and hopelessly inoperable. Both glandular and epidermoid cancers occur in this locality, the latter being the more frequent. We would emphasize here the necessity of early diagnosis not only in these cancers but in all those found about the external genitalia. The cases are not infrequently considered trivial in their early stages because of the lack of pain and other definite symptoms. They are often mistaken for venereal lesions, especially chancroids. If the patient is unfortunate enough to show a positive Wassermann reaction, an erroneous diagnosis is particularly likely to be

made. A characteristic of cancer in these areas is that the lesion bleeds easily upon slight trauma, is firm to the touch and increases in size with considerable rapidity. Any lesion which is suspicious, developing in a woman over thirty five years of age or even younger, should be submitted to biopsy unless its malignant character can be absolutely excluded. It is only by securing these cases early that a higher percentage of five year salvage can be obtained. In many of our cases only mild symptoms have been present, even when moderately advanced, and one or two instances have been entirely silent.

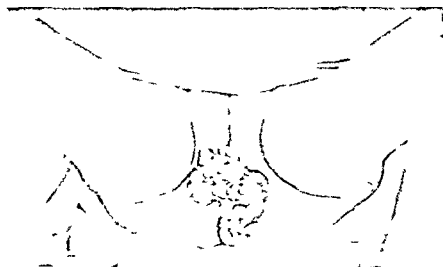


Fig. 173 —Extensive carcinoma of the perineum, fourchette and anal region with wide spread metastasis

Dysuria itching burning local pain and, in advanced cases, incontinence may be present. In most of our cases the treatment has consisted of the implantation of bare tubes into the lesion and in our earlier cases radium packs to the inguinal glands. More recently the radium packs have been discarded for the use of deep x-ray therapy. In some of the earlier cases the inguinal glands have been removed en bloc, the excision following by implantation of bare tubes and subsequent deep x-ray therapy. In nearly all cases improvement in the local condition has occurred and in the majority complete local healing. It is as yet too early to prognosticate the percentage

of five year cures. The dosage in the primary lesions depends considerably upon the size of the tumor. It is preferable however to use bare tubes of about 0.6 to 1 millicurie and to place these  $\frac{1}{8}$  inch apart through the base of the lesion and around its edges. It must be remembered that bare tubes continue to give off emanations for one hundred and thirty two hours and bearing this in mind and using it as an example to follow, if the total amount of radium from 6 bare tubes approximates 4.2 mc. the total dosage will be  $4.2 \times 132$  or 528 millicurie hours. In the small lesions this dosage might be sufficient and if it is not it is usually repeated. As in dealing with all malignant conditions treated by irradiation a careful and conscientious follow up is essential. These cases are observed at three week intervals for the first three months and later at six week intervals providing they are doing well. Whether or not a second or even a third application of radium is indicated can be determined by the response of the tumor to the first treatment. Furthermore occasional small areas are observed which have failed to receive adequate irradiation and these should be treated as soon as discovered. If there is an undue local reaction following irradiation frequent flushing of the genitalia with warm saline solution and the liberal application of sterile vaselin will tend to minimize the attending discomfort.

**Carcinoma of the vulva** may be glandular or epidermoid in type but is usually the latter. Our cases have varied in size from  $\frac{1}{2}$  cm. in diameter to complete involvement of both labia urethra and perineum. This condition is usually primary but we have encountered 1 case of secondary involvement in which the primary tumor was located in the cervix. This case was too advanced to permit of even palliative treatment. Early cases should be treated with bare tubes with the same dosage per cubic centimeter as that previously described for cancer of the urethra. Excision of the inguinal glands should be followed by the implantation of bare tubes with subsequent deep x ray therapy to this region. Early metastasis is common. Frequently treatment is given in our clinic to the evidently hopeless cases using small doses of radium. This is given not so much



Fig 174 —Carcinoma of the vulva before treatment

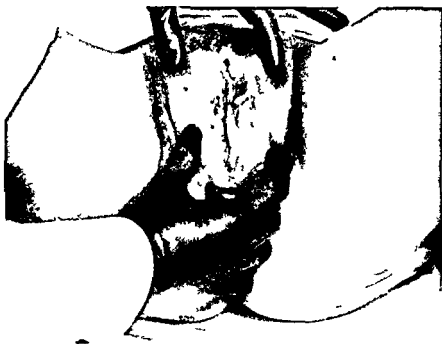


Fig 175 —Showing results of irradiation six weeks later. This patient was treated with bare tubes of approximately 500 millicurie hours



with the expectation of cure as with the hope of relieving the local symptoms. One or 2 such cases have however been encountered in which the tumor responded so well to irradiation that a second larger dosage was successfully given. At best the percentage of five year salvage is small in carcinoma of the vulva. The ideal treatment in the early cases is we believe wide excision of the local lesion and the implantation of bare tubes. The inguinal glands should be excised en bloc regardless of whether



Fig 176 —Carcinoma of both labia perineum anal region and inner aspect of thighs. Wide spread metastasis. Case too advanced for treatment.

or not palpable enlargement is present. Subsequently a complete cycle of deep x ray therapy to both inguinal regions should be given.

Carcinoma of the vagina may be either primary or secondary. The primary lesion is comparatively infrequent while involvement secondarily from the cervix is frequent. The tumor may be ulcerative or papillary in type the secondary form tending to become ulcerative in its later stages. In early primary le-

sions the choice of treatment depends considerably on the site of the tumor. If it is situated in a position in which a radical excision is possible this is the method of choice followed by implantation of bare tubes. Frequently however the neoplasm develops in a locality in which radical removal is impossible. In these cases the insertion of bare tubes is indicated. Tubes containing 0.5 to 1 millicurie each are inserted as heretofore described throughout the tumor and about its edges. The inguinal glands should also be treated unless the tumor is situated high in the vagina. Deep x-ray therapy should follow within four to six weeks after irradiation. Secondary carcinoma of the vagina should be treated during the course of the application of the primary lesion to the cervix and will be considered under that heading. As stated primary carcinoma of the vagina is a relatively infrequent form of neoplasm. We have encountered but 1 case in our service at the Philadelphia General Hospital, this tumor was 3 cm. in diameter presenting the usual characteristics of an ulcerating malignant lesion. The cervix was normal as was the remainder of the genital tract. This case was treated by irradiation a year ago so that the ultimate outcome is uncertain. No evidence of the disease was present at the last follow up examination and complete local healing had occurred.

**Carcinoma of the cervix** is the most frequent form of malignant neoplasm encountered in the female genital tract, it has practically no age limits although the majority of cases are observed between thirty five and fifty five years of age. It is relatively infrequent in nulliparous individuals and is especially prone to develop in cervixes which have been the seat of a long standing low grade infection. Early diagnosis is difficult, while late diagnosis is easy, but of little value. The only symptoms of importance are hemorrhage and discharge. The cervix is poorly supplied by the sensory nerves and pain generally indicates the extension of the tumor beyond the confines of this organ. Hemorrhage is by far the most important symptom. It is intermenstrual, of the type commonly described by the laity as "spotting" bright red in color, and tends to follow trauma, gynecologic examination, coitus, straining at stool, and is rather

rapidly progressive in type. It is usually of a small amount at the onset although occasionally cases are encountered in which erosion into a large vessel produces massive hemorrhage in the early stages of the disease. Discharge is probably the primary symptom in the majority of cases. The fact however that the disease usually develops in cervixes which are the seat of infections producing leukorrhea greatly nullifies the diagnostic value of this symptom. The fact that the discharge is not a new symptom but merely the augmentation of an apparently chronic process which has been present for years tends to make patients disregard its significance. The cervix is an easily accessible organ and may be readily palpated and inspected but even to the experienced gynecologist the recognition of extremely early cancer may be difficult without the aid of a microscope. This is particularly true in those cases in which the disease develops in an area of previous erosion or within the cervical canal. The fact that the disease is prone to develop about the time of the menopause when more or less irregularity is expected by every woman tends to prevent patients from seeking early aid. It is a not uncommon practice to blame the general practitioner for the lateness with which these patients are commonly seen by the surgeon yet in many cases this is unjust. It has been our experience that between three and six months elapse in the average case before the patient seeks relief. This period is frequently sufficient for the tumor to develop beyond the range of operability. No satisfactory treatment of carcinoma of the cervix is at present known. The ultimate mortality varies from 50 to 90 per cent. There is urgent need for some uniform classification of these cases as well as for further study of end results. At present a satisfactory comparison of the end results as secured by various clinics is almost impossible because of the different standards of cure and the different methods of presenting statistics. A five year standard of cure is we believe the preferable one. The important point is how many five year cases have been encountered and how many of these are alive at the conclusion of this period. The next important point is the method of treatment which has been employed. Another

point on which uniformity is desirable is the method of dealing with untraced cases. The method suggested and generally followed in Europe of counting all untraced cases a dead has much to recommend it as it stimulates a thorough follow up. On the other hand this method is distinctly unfair to the American surgeon. In Europe with their strict registration law it is usually possible to trace the large majority of cases. In this country however with its floating population and all absence of strict registration law a relatively large proportion of five year cases are certainly untraceable. The method recently suggested by Ward of New York of excluding all such cases from their follow up is preferable. Some uniform method of classification of the stage of advancement at the time of the initial treatment is also necessary.

The classification suggested by Schmitz has been the one employed by us. This divides carcinoma of the cervix into five groups viz

Group I—In which the disease is apparently confined to the cervix

Group II—Cases of border line operability

Group III—Clearly inoperable cases

Group IV—Cases in the terminal stages of the disease

Group V—A recurrence following attempts at radical removal

This classification has the advantage of simplicity and is based upon clinical findings. It is practically that adopted by Greenough of the American College of Surgeons and is employed by Ward of New York and in the Gynecologic Department of the Hospital of the University of Pennsylvania. Considerable difference of opinion still exists as to the ultimate advantage of irradiation and hysterectomy in the treatment of carcinoma of the cervix. The general trend we believe however is toward irradiation.

In the Stage I cases irradiation and radical hysterectomy produce practically equivalent results. In all other cases however irradiation is definitely superior, not only as a palliative but as a curative measure. Early in the history of radium

therapy it was discovered that certain tumors responded more favorably to its influence than did others. As a general rule the more embryonal the type of tumor and the higher the percentage of embryonal cells contained in the neoplasm the more favorably does the tumor react and respond to adequate irradiation. On the other hand the embryonal tumors are as a general rule the more malignant exhibit more rapid growth and produce the earlier metastasis. A study by Kimbrough of the cases of carcinoma of the cervix occurring in the Gynecologic Department of the University of Pennsylvania has shown definitely that in the embryonal variety of cervical carcinoma *i. e.* the basal and transitional cell forms there is earlier and more complete local healing found than in the more adult type of tumor such as the squamous cell and the adenocarcinoma. However this is more of theoretical than practical value as a careful study of the end results fails to show any material difference in the five year salvage of the varieties of the tumor encountered. The greater malignancy and the earlier metastasis developing in the embryonal forms probably counterbalance their greater susceptibility to irradiation. The more embryonal types of tumors grow more rapidly and hence are likely to be more advanced when first observed. These tumors also show a somewhat higher percentage of early local healing following irradiation than do the riper forms of malignant neoplasms. As a general rule the papillary form reacts more favorably to treatment than the ulcerative or interstitial types. The cases observed in the Philadelphia General Hospital were nearly all in Stages III, IV and V. In the Stage I cases 2400 millicurie hours of radium applied to the cervix either in the form of element or properly screened emanation is the usual method of choice. In many instances a high amputation of the cervix is performed with the cautery and followed immediately by irradiation of the cervical stump. In some instances it may be necessary to free the bladder from the anterior uterine wall pushing it away from the field of irradiation while the radium is *in situ*. One of the dangers of irradiation is injury to the bladder or rectum. Packing these structures out of harm's way by means of gauze packing is an

doubtedly the best safeguard. A second application of similar dosage is often used two or four weeks later, and in some instances a third or even a fourth application may be indicated depending upon the local and general reaction.

The Stage II cases are treated practically the same as are the Stage I.

Stage III cases. When the disease is thus far advanced the ultimate prognosis is generally unfavorable. Fortunately, however, a few may be permanently cured. Much benefit can generally be secured so far as the local lesion is concerned. Hemorrhage and discharge can usually be checked and as a result the symptoms incident to the former disappear, cellulitis of the broad ligaments is alleviated, and improvement in the general health occurs. Such patients are frequently able to resume their normal life despite the fact that the deeper portions of the tumor may still be developing. In 70 per cent of all cervical carcinomata complete local healing was secured.

Stage IV cases are rarely amenable to any form of x ray or radium therapy. Attempts at irradiation are prone to aggravate the lesion and result in a high percentage of vesical or rectal fistulae. It is only the exceptional case that receives any irradiation in our clinic.

Stage V cases are as a rule, best treated with bare tubes. In the case of carcinoma developing in the cervical stump following a supravaginal hysterectomy the application of the element or a properly screened capsule containing the equivalent of 50 to 100 mg of radium inserted into the stump for eighteen to twenty four hours is generally employed. One of the dangers in these cases is that an adherent loop of intestine may be present at the upper end of the cervical stump and damage may be done to it. When a second irradiation is to be used bare tubes or radium bearing needles are generally employed and are applied to the lesion for a distance of 1 cm beyond the edge of the carcinoma. At the Philadelphia General Hospital it has been our custom to employ routinely deep x ray therapy in all cases of cervical carcinoma in which any hope whatever is present of an ultimate cure. In our early cases this was followed by a

rather high percentage of reactions. Later, however, as a result of improved technic, these unpleasant sequelæ have almost disappeared.

**Carcinoma of the Body of the Uterus**—This disease occurs somewhat later than carcinoma of the cervix and is relatively as frequent in spinsters as in multipara. Irregular bleeding of the



Fig 177—Adenocarcinoma of the fundus with small myomata. Actual size. Diagnostic curettage and 2400 millicurie hours. Radiation followed ten days later by panhysteromyomectomy and bilateral salpingo-oophorectomy. Patient well and no evidence of recurrence three years later.

metrorrhagic type and leukorrhea are the chief, and often the only, symptoms except in the advanced stages. Bleeding tends to follow trauma, is painless, and bright red in color. However, owing to the protected locality in which the disease develops the tendency of the bleeding to follow trauma is somewhat less marked than cervical cancer. The discharge is watery, irritant, and soon becomes malodorous. The discharge in cases of fundal

carcinoma is somewhat more pronounced than in the cases of cervical neoplasms. Probably, on account of the encapsulated region in which the disease develops, the ultimate salvage is somewhat greater in these cases than when the disease develops in the cervix. In the early cases diagnostic curettage must often be resorted to. The Clark test which consists in the introduction of a sound, the gentle raking over of the endometrial surface with the tip of the instrument, is of distinct value. This procedure may be employed in the office, provided rigid asepsis is observed. Carcinoma is a friable vascular growth,

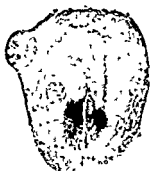


Fig 178 —Small myomatous uterus. Hyperplasia of the endometrium and adenocarcinoma of the cervico uterine junction. D and C. Irradiation 2400 millicurie hours. Panhysterectomy two weeks later. In this case cancer was not suspected prior to the histologic examination of the curettings. Note the area of acute radium reaction.

hence, bleeding follows this test. The test, although not absolutely diagnostic, is of distinct value and, on account of its simplicity, may be recommended in all suspicious cases. While curettage has some theoretic disadvantages, especially in view of the work done by Sampson, it is, nevertheless, often the only method by which an early diagnosis can be reached. Early diagnosis is essential in these cases, and a recent review of 101 cases in the University Hospital by the authors show but 34.5 per cent. of cases alive at the end of five years. This series includes cases in all stages of advancement. The diagnosis is



more readily made in women who have passed the menopause than in younger individuals. The cases in which diagnostic curettage is performed should have a dosage of 2500 millicurie hours of radium applied to the fundus. Adenocarcinomata of the fundus are composed of a moderately adult type of cell and hence require a somewhat larger dosage than does cervical cancer. In all cases in which operation is not contraindicated panhysterectomy with bilateral salpingo oophorectomy is the method of choice. When a preliminary curettage has been done followed by irradiation hysterectomy may be performed two or three days after the preliminary treatment. If the radical operation is absolutely contraindicated the preliminary irradiation should be followed in two weeks by a second irradiation of like dosage. To emphasize the difficulty of treating carcinoma of the fundus we may state that at present we have two uteri: one removed at autopsy and one removed at a subsequent operation. One presents definite evidence of radium necrosis in the center of the uterine canal while the neoplasm was situated in the right cornu; the other specimen showed a radium reaction low in the endometrial cavity, the neoplasm being situated at the top of the fundus. Cases of carcinoma of the fundus should be kept under observation and when irradiation only has been performed the Clark test should be employed every two months. If bleeding follows the manipulation of the sound another radium application is indicated.

**Carcinoma of the Ovaries**—This disease is essentially a surgical one, a proportion of cases being unrecognized prior to the histologic examination of the neoplasm. We have personally had very little success in the treatment of this condition by either radium or x ray. A number of undoubted cases are however on record in which definite palliation and even cure has been secured by the deep x ray therapy. This is especially true in the work emanating from the Memorial Hospital in New York. Two years ago a case of this kind was encountered by one of the authors. The patient had had a hysterectomy and bilateral salpingo oophorectomy for carcinoma which involved both ovaries. This diagnosis was verified by a histologic exami-

nation One year after operation evidence of a recurrence developed When seen by the author, bilateral tumors, one the size of a fetal head and the other the size of a small orange, and ascites, were present The case was evidently a hopeless one from the operative standpoint, and was referred to Dr Pancoast of the University Hospital for deep x-ray therapy Under x-ray therapy both the tumors diminished in size, the ascites disappeared, and eleven months after the first x-ray treatment

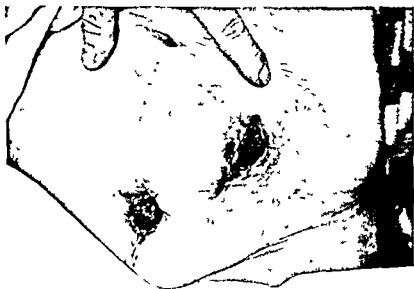


Fig 179—Adenocarcinoma of both ovaries This patient had two abdominal sections performed at different hospitals Both operations failed to remove either of the tumors, and in both cicatrices implantation carcinoma developed These were papilocystic, purplish, friable and resembled ovarian neoplasms This case demonstrates the necessity for wound protection and the removal without rupture or tapping when performing oophorocystectomy for malignant ovarian tumors

no evidence of the disease could be demonstrated by bimanual examination The patient gained considerably in weight, and was symptom free One or two somewhat similar cases have also been encountered, so that, while the usual results of x-ray treatments are unsatisfactory, this method is at least worthy of a trial in non-operable cases and should, we believe, be employed routinely as a postoperative measure The x-ray cycle can usually be begun three to six weeks after the hysterectomy

## GROUP IV COMPLICATIONS ENCOUNTERED

In the application of radium to the pelvic organs there is little reaction encountered except when large dosages are employed a hypersensitive patient may show some slight reaction after a dosage of 1200 millicurie hours but this is unusual Practically all the reactions take place before the removal of the ra-

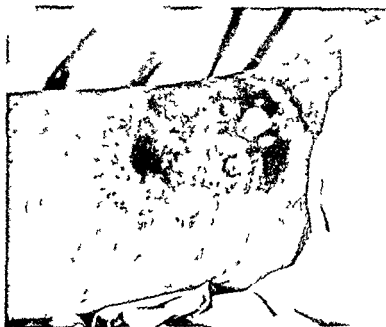


Fig 180—One of our early cases illustrating a radium burn of left thigh following treatment for cervical carcinoma. At that time radium packs were employed to radiate the parametria. The patient removed the pack from its original position and turned it upside down on her thigh with the above result. Photograph taken two months after the accident.

dium the most common being nausea vomiting pelvic pain and slight elevation of temperature. The latter seldom rises beyond 99° or 100° F and then quickly subsides. In cases such as endocervicitis and myopathic hemorrhage there is usually no reaction. A moderate discharge frequently follows the application of radium to the uterus. If the radium has been correctly applied and proper dosage employed bladder and rectal symp-

toms rarely occur. Rectovaginal or vesicovaginal fistulæ rarely develop, and in properly treated cases irradiation may be looked upon as a safeguard against these complications. They are more prone to develop in cases in which irradiation has been applied during the advanced stages of the disease. Fistulæ are probably the most serious complications encountered. Careful packing away of both bladder and rectum from the seat of irradiation, and the keeping of these structures empty during the time the radium is in place, are of the utmost importance. If fistulæ have developed it is wisest not to attempt repair for a considerable period of time due to the devitalization of the tissues incident to irradiation. We have had one death which could be definitely ascribed to the use of radium. This was a patient thirty eight years of age in Stage III of carcinoma of the cervix. Under anesthesia biopsy was performed and 2400 millicurie hours of radium inserted into the cervix. There was a mild reaction in the form of nausea and vomiting which disappeared on the second day. On the fourth day the temperature reached  $104^{\circ}$ , and the pulse was accelerated. No other symptoms were complained of, nor were any signs of peritonitis present. The pulmonary findings were negative. On the fifth day the temperature rose to  $101^{\circ}$  in the morning with sudden distention of the abdomen and the patient died three hours after the tympanites was first noticed. Autopsy revealed a rupture of the small abscess in the left ovary, inducing a peritonitis.

#### GROUP V AUTOPSY MATERIAL AND FINDINGS

Because of the system employed in the Philadelphia General Hospital postmortems are the rule rather than the exception when deaths occur. The following paragraphs will be indicative only of the general findings in each type of case to date. There have been no deaths following irradiation for benign lesions and no autopsy findings in such cases are available.

As a rule malignant tumors of the urethra show destruction of the tissues in the region of the external urinary meatus. In 1 case a small area of carcinoma implant was found in the right ureter, pressing on the ureter in the broad ligament. Because

of interference with the kidney and bladder function hydro ureter and hydronephrosis are common complications As the anterior vaginal wall is implicated through extension of the disease the vesicovaginal septum may also be involved In cases of epithelioma of the vulva with mild or wide spread unilateral or bilateral extension even the perineum or upper thighs may be involved These cases may be mistaken for syphilis or granuloma inguinalis In case any doubt exists biopsy and the Wassermann test should be employed It must also be remembered that because the Wassermann test is positive it does not preclude the possibility of cancer being present We have seen many advanced cases of carcinoma of the external genitalia which have been treated for syphilis over a prolonged period due to this complication

Carcinoma of the vagina as previously stated may be primary or secondary It is most frequently an extension from cervical tumors It is generally of the epidermoid type and responds moderately well to irradiation with bare tubes In cases of carcinoma of the cervix it is not unusual at autopsy to find absolutely local healing of the cervical and vaginal lesions but involvement of the parametrium hydro ureter and hydronephrosis and other extensive intraperitoneal invasion It would seem that in these cases the radium cured the local lesion but that in the depths of the tissues the disease continued to develop Carcinoma of the ovary gives early metastases and implants in the abdominal wall are occasionally observed The disease may be secondary to carcinoma of the upper abdomen notably the Krukenberg tumor which is secondary to gastric carcinoma For this reason in operating upon ovarian carcinoma the upper abdomen should always be examined as a preliminary step Ovarian carcinoma may also be secondary to carcinoma originating in the uterine cavity The work of Sampson has demonstrated the transtubal migration of portions of the normal endometrium We have ourselves demonstrated particles of carcinomatous tissue free in the tubal lumen in specimens of fundal carcinoma which have been removed by hysterectomy and have seen 1 case which we feel sure was an ovarian implant

due to this method of extension. For this reason, when performing diagnostic curettage, special care should be observed to secure a wide dilatation of the cervix and to avoid a piston-like action when inserting instruments, packing, or rubber tube bearing radium into the fundus. For the same reason irrigation of the uterine cavity following curettage is inadvisable

#### GROUP VI. RARE CASES

Very brief mention will be made here of certain unusual cases which have been observed in the Radiologic Department of the Philadelphia General Hospital:

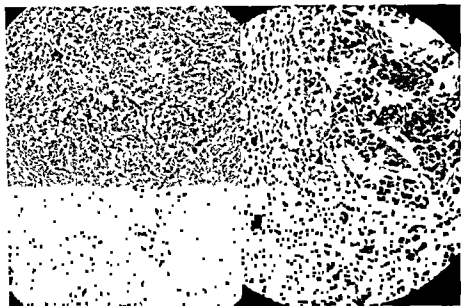


Fig 181

Fig 182

Figs. 181, 182 —Illustrating by low power (Fig 181) and high power (Fig 182) the case of melanotic sarcoma described in the text

**Case I.**—Patient seventy-six years of age was admitted to the Radiologic Ward in a moribund condition and died within one hour. No history was obtainable. Postmortem examination revealed extensive metastases of practically every organ of the body including the caseous system, by a melanotic sarcoma which was probably primary in the vulva. The size of the

original neoplasm was not known but the vulva on both sides presented moderately advanced lesions. These tumors had not destroyed the entire vulvar tissue so that orientation was still possible. The uterus, tubes, ovaries, bladder, rectum and peritoneal surface were studded with uncountable melanomata.

**Case II**—Patient forty two years of age complained of moderate metrorrhagia and occasionally menorrhagia. Diagnostic curettage was performed and a moderate amount of tissue secured. *2500 millicurie hours of radium was applied to the uterine cavity.* Histologic examination showed an adenocarcinoma of the fundus. Twelve days after the preliminary curettage a hysterectomy and bilateral salpingo oophorectomy were performed. At this time the entire pelvis was filled with adhesions, bilateral pyosalpingitis and bilateral ovarian abscesses were present; the adhesions were unusually dense in character and the general impression conveyed was one of an old chronic pelvic peritonitis. The interesting point in this case is that although a full dosage of radium had been applied, absolutely no reaction at any time developed following the procedure. The temperature never rose above 99° and no pain or tenderness were experienced. This case is instructive in that the presence of inflammatory lesions in the adnexa do not always result in the development of acute peritonitis, even though massive irradiation is employed. However, this is not to be understood as indicating that irradiation may be safely employed when adnexitis is present. However, it proves that an acute flare up does not always develop under such circumstances and it is possible that exacerbations occur only when viable pathologic organisms are present in the adnexa. Its well known encapsulation tends to destroy such microorganisms. It seems probable that occasionally in any large series of myomata submitted to irradiation the presence of adnexitis must be overlooked and yet in our review of a fairly large series of such cases acute exacerbation was found to be an extremely rare occurrence.

## CLINIC OF DR FIELDING O LEWIS

PHILADELPHIA GENERAL HOSPITAL

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### TREATMENT OF CANCER OF PARANASAL SINUSES, TONSILS, AND LARYNX

THE results obtained in the treatment of cancer involving these structures depends upon the early recognition of the disease and the prompt institution of rational treatment, by so doing our efforts are many times rewarded by a most gratifying and pleasing outcome

**Case I Adenocarcinoma of the Left Maxillary and Ethmoidal Sinus**—Male age fifty nine machinist by occupation, born in England He was admitted to the hospital on October 5 1922 His chief complaint at that time was epistaxis complete stenosis with continuous secretion from the left nostril and partial deafness of the left ear extending over a period of one year

The hospital records taken at the time of his admission give the following notes as to his present illness His symptoms began about one year ago by severe bleeding from the left nostril, following which it became completely obstructed The epistaxis has recurred numerous times since There has been no pain in the nose or in the forehead There has been no cough or sneezing

*Personal History*—Has had the usual diseases of childhood denies venereal infection

*Family History*—Mother dead cause unknown Father killed in an accident Five sisters living and well No history of cancer or tuberculosis

General physical examination revealed nothing of an organic nature On examination of the nose, the alæ of the left nos



tril was found inflamed and reddened associated with a clear watery discharge There was some evidence of external deformity the left side of the nose being more prominent than the right The left nostril was filled with a substance neoplastic in nature which bled easily The right nostril was apparently normal

Transillumination of the paranasal sinuses showed a darkened area in the frontal region The right maxillary antrum was clear but the left antrum was dark x Ray examination shows that the patient has apparently no frontal sinuses The ethmoids are normal Right antrum is normal The left nares and antrum present a dark shadow which is no doubt due to a new growth Blood Wassermann was negative The blood picture is that of a secondary anemia with only 60 per cent hemoglobin and 3 780 000 blood cells Urinalysis was likewise negative in spite of his having been an alcoholic He is badly in need of oral hygiene and the extraction of a few old roots The teeth in relation to the left maxillary antrum were negative His temperature chart which you will observe is practically normal A portion of the nasal growth was removed for pathologic study the report of which was adenocarcinoma

The problem which confronted us at the time was what form of treatment would offer the patient the best chance for relief From examination the growth seemed to be primary in the antrum *the naso-antral wall was partially destroyed and there was possibly some involvement of the anterior ethmoidal cells* As radium had been used successfully in this type of carcinoma we decided on a combined surgical and irradiation treatment

On October 16 1922 just about four years ago under ether anesthesia an incision was made through the cheek beginning just below the eye and extending down to the alar exposing the bone The soft tissue and periosteum were reflected outward exposing the outer wall of the antrum The antrum was opened by means of a chisel and as much of the neoplasm removed both from the antrum and nasal cavity as possible This operation was devised by Doctor Crosby Greene of Boston with a view of making a permanent opening through the cheek into

the antrum so as to admit thorough inspection from time to time, and if necessary for the repeated applications of radium. After the removal of the growth bare tubes of radium were inserted into the region of the ethmoids and a capsule of 100 mg. was placed into the antral cavity. This patient has had three other similar applications since his operation, and radium plaques have been applied to both sides of the neck. There was no evidence of metastasis at any time in the cervical lymphatics. The patient has made a satisfactory recovery, and at the present examination there is no evidence of recurrence. The opening



Fig 183.—Case I. Adenocarcinoma of the left maxillary and ethmoidal sinuses. Treatment by Crosby Greene method. No evidence of recurrence after four years. Antral opening obscured by cotton pledget.

into the antrum is still patulous, which, I believe, can now be closed with safety by plastic operation.

Other forms of carcinoma, which are found in this region, are not so amenable to this form of treatment, and the prognosis is always very grave.

**Case II. Prickle-cell Carcinoma of the Left Maxillary Sinus.**—The next patient is a woman forty-seven years of age, representing a lesion in the same location, but of a different type.

tril was found inflamed and reddened associated with a clear watery discharge. There was some evidence of external deformity the left side of the nose being more prominent than the right. The left nostril was filled with a substance neoplastic in nature which bled easily. The right nostril was apparently normal.

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The problem which confronted us at the time was what form of treatment would offer the patient the best chance for relief. From examination the growth seemed to be primary in the antrum the naso antral wall was partially destroyed and there was possibly some involvement of the anterior ethmoidal cells. As radium had been used successfully in this type of carcinoma we decided on a combined surgical and irradiation treatment.

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Fig 184 —Case II Perikle cell carcinoma of the left antrum with involvement of the alveolus and hard palate



Fig 185



Fig 186

Fig 185 —A case representing squamous cell carcinoma of the right maxillary sinus. Treated by electrocoagulation and radium

Fig 186 —A case representing squamous cell carcinoma of the right maxillary sinus in which only palliative treatment is indicated

sloughing of the tonsillar area and the involved side of the tongue

You will observe that the area has entirely healed. There has been almost complete retrogression of the lymph nodes and there is no evidence of recurrence. The patient has gained in weight and feels perfectly well.

Carcinoma of the tonsils seem to be particularly more favorably affected by radium than carcinoma in other parts of the mouth. Our results have been most encouraging and it is my belief that carcinoma of the tonsils should be treated by radium in preference to surgery if seen early enough for a curative treatment.

Of the 66 cases of carcinoma of the tonsils which have reported to the clinic only about 30 per cent were suitable for probable curative treatment. Of the 20 cases 50 per cent or 10 are still living and in good condition.

#### CARCINOMA OF LARYNX

The next group of cases which I have the privilege of demonstrating are cases of laryngeal carcinoma. Laryngeal cancer one of the saddest afflictions with which the laryngologist has to deal has for many years been a difficult problem still is and *perhaps will continue to be since it is apparently on the increase* and the mortality is high. Laryngologists and general practitioners must marshal every means at their command to stop its progress. It can be permanently cured when seen early provided an early diagnosis is made and the proper treatment immediately instituted.

The classification of laryngeal cancer given by Krishaber in 1879 should be well understood. As pointed out by Thompson the results of surgical treatment does not depend upon the histologic structure but entirely upon the site of origin.

The familiar classification is first intrinsic arising from the vocal cords, ventricles, ventricular bands, interarytenoids and subglottic area and second extrinsic arising from the epiglottis, arytenoids, aryepiglottic folds, pyriform sinuses and pharyngeal surface of the cricoid cartilage.

Statistics show that the intrinsic forms are the types most frequently seen, and that the vocal cords are the structures more often primarily involved. It develops slowly and metastasis is late, due to the confined arrangement of the laryngeal lymphatics.

The extrinsic forms on the other hand have a more rapid course and metastasis occurs early, which does not mean, however in my opinion that all extrinsic cases are by any means a hopeless condition. In all cases of chronic hoarseness and all cases of slightly impaired voice in adults due to an infiltrating process of the vocal cords or a neoplastic formation, regardless of its location cancer should be excluded. While it usually occurs in patients past the age of forty, yet it is not infrequently found in patients under thirty years of age. I have performed total laryngectomy in two young men and one young woman under the age of thirty, who had extrinsic laryngeal carcinoma.

A very small percentage of those suffering from laryngeal cancer in this country are seen by the laryngologist during the incipient stage, in other words when the disease is limited to the vocal cords. In this clinic 75 cases of laryngeal carcinoma have been examined during the past five years. Not one of these were limited to the vocal cords or suitable for laryngofissure, due no doubt to the fact that little or no inconvenience was experienced by the patient except the sole symptoms of slight hoarseness, and regarded by himself, as well as often by his physician, as being due to an acute laryngitis. Seldom are these patients examined by skilled laryngologists until other and more distressing symptoms appear.

In extrinsic laryngeal cancer occurring in phlegmatic individuals, unfortunate for them the first symptoms noted is often a "lump in the neck," when the laryngoscopic examination will reveal an infiltrating process in the larynx or beyond the laryngeal box, being another strong argument in support of a periodic physical examination. Pain or throat ache may be an early symptom especially in those whose occupations require an excessive use of the voice. It is usually, however, associated with a later stage, when dyspnea, dysphagia, marked enlargement of

the cervical glands foul breath and cachexia are present A diagnosis at this stage is not difficult and usually means a hopeless outlook

All sorts of laryngoscopic appearances as to color location and whether the mobility of the cord is or is not impaired in early laryngeal cancer is described in the literature The same may be said of benign neoplasms I would therefore advise that all such cases be studied by a laryngologist in conjunction with an accomplished internist pathologist bacteriologist roentgenologist and serologist

The differential diagnosis between carcinoma syphilis and tuberculosis is often a difficult matter One must bear in mind that the three conditions may be present in the same larynx It is not unusual to find a carcinoma develop in a syphilitic larynx A positive Wassermann should not always be a final conclusion in a laryngeal lesion Much valuable time is often lost by instituting a long antiluetic treatment without proper observation Biopsy as a means of diagnosis has long been a debated question among laryngologists It is in my opinion a good rule to follow in doubtful forms of neoplasm of the larynx If a biopsy is performed and the tissue examined by a careful and experienced pathologist the results are usually convincing especially if one has sufficient clinical evidence Mistakes which are sometimes made and biopsies poorly done is no reason why the surgeon should place explicit confidence in a negative biopsy In extrinsic carcinoma the diagnosis is not so difficult In intrinsic carcinoma repeated and careful laryngeal examination together with one's clinical experience is an invaluable means of reaching a definite conclusion It is our practice to make a biopsy in all cases

Twenty years ago the eminent English surgeon Doctor Charles P Childe wrote his book about cancer in advocacy of the theory that many lives could be saved if persons in the early stages of that disease would apply to physicians in time to make a cure possible Since that time much has been done

Some years before that Morell Mackenzie stated that the only possible termination of any laryngeal cancer was usually

death, that the usual duration of epithelioma of the larynx appears to be about eighteen months" Much has been observed and accomplished to definitely refute that statement. The whole world has joined forces to combat its progress. Research institutions have been established to investigate the cause of cancer and if possible discover a means to stop its advance. Diagnostic methods have been improved. Surgical technic has been established to a high point of excellency. Radium and Roentgen ray have been introduced for the cure of cancer and for its palliation. Numerous forms of treatment have been advocated, usually empirical. A vast amount of constructive study has been carried out. A systematic form of instructions is being given to the public in the early signs of cancer and the medical profession at large are being aroused to use every means at their command for its early recognition.

In 1925 over seventy eight thousand persons died of cancer in the United States. If we accept the previous statistical proportions, about 5 per cent of this number died of cancer of the larynx, a percentage which, I predict, will be greatly reduced in the very near future. The seed sown by the recent propaganda is, I believe, already beginning to bear fruit, as evidenced by the public's interest in yearly physical examinations and a general interest and alertness of the medical profession in general.

Operable cases of cancer of the larynx should, in my opinion, be treated surgically when possible. Our experience with radium and Roentgen ray in the treatment of laryngeal cancer has been disappointing. My experience coincides with that of the Spanish surgeon, who states "that in most cases treatment of laryngeal cancer with radium or Roentgen ray fails to arrest the progress of the disease. It may, on the contrary, aggravate the cancer, or by impairing the condition of the skin, prevent or complicate radical operation. Irradiation should be limited, in my opinion, to inoperable cases or to those in which operation is refused." It is, however, of valuable use for the postoperative treatment of extrinsic cancer.

**Treatment**—In my opinion, only two forms of procedure



should be considered in operable intrinsic cancer laryngofissure, for those limited to the vocal cords, and total laryngectomy for all others. Endolaryngeal removal is not to be recommended in spite of reported cases in which this method has been success

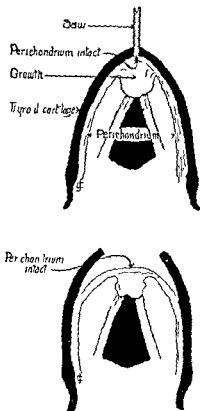


Fig 190—Chevalier Jackson's method of subperichondrial dissection in anterior commissure growths. Procedure in cases in which the cancerous growth is in the anterior commissure. The shears are not used for fear of cutting the growth. The thyroid cartilage is sawed through without injury to the inner perichondrium, which is then dissected backward, safely beyond the posterior limits of the growth.

ful, because the extent of the lesion cannot be determined by preoral examination. Partial or hemilaryngectomy, because of its high operable mortality and high percentage of recurrences, is now seldom employed. Laryngofissure is the treatment of

choice in early intrinsic cancer; that is, when the growth is limited to the anterior two-thirds of the cord, circumscribed and of slow growth. St. Clair Thomson states: "My statistics show a lasting freedom of disease in many cases of five to fifteen years in 80 per cent. of cases." Jackson reports 79 per cent. of cures.

Operators differ slightly in the technic of this operation, some preferring tracheotomy and packing the larynx after



Fig. 191.



Fig. 192.

Fig 191.—Case I. Laryngeal carcinoma of larynx. Laryngectomy performed November, 1921, for extrinsic carcinoma of the larynx, showing end of esophagus attached to the skin of the neck with feeding tube in place

Fig 192 —Photograph of same patient as shown in Fig 191, after plastic operation on esophagus. The patient is living after five years without recurrence

excision of the growth, while others expose the trachea, omit tracheotomy and packing unless complications arise. I prefer the destruction of the growth by fulguration instead of excision, as this method prevents hemorrhage, lessens pulmonary complications, and usually obviates tracheotomy.

For those cases in which the disease has extended beyond the vocal cords total laryngectomy is, in my opinion, the only



Fig 193



Fig 194

Fig 193 —Case II Carcinoma of the larynx Age thirty four Laryngectomy in February 1922 No evidence of recurrence to date

Fig 194 —Case III Woman with carcinoma of the larynx Total laryngectomy in February 1923 No evidence of recurrence to date



Fig 195



Fig 196

Fig 195 —Case IV Carcinoma of the larynx Age twenty nine Total laryngectomy in October 1923 No evidence of recurrence

Fig 196 —Photograph of larynx removed from Case IV showing extensive involvement



Fig 197



Fig 198

Fig 197 —Case V Carcinoma of larynx Total laryngectomy July 1925  
No evidence of recurrence Fair buccal voice

Fig 198 —Case VI Age fifty two Total laryngectomy June 1924  
Has developed a splendid voice



Fig 199



Fig 200

Fig 199 —Case VII Total laryngectomy in February 1925 Has recently developed a carcinoma of the tonsil which is thought to be independent of his laryngeal carcinoma

Fig 200 —Photograph of the larynx removed from Case VII

means of a possible cure. Without this procedure the mortality is almost 100 per cent. Previously the mortality from the operation was extremely high, but now, with the improved technic and improved methods of postoperative treatment, the mortality is becoming notably less.

I have the privilege of showing you a number of these post-operative cases of those who are now perfectly well two to five years after operation. They are quite happy, have resumed their occupations and are useful citizens who, without this radical



Fig 201



Fig 202

Fig 201.—Case VIII. Physician. Age seventy six. Total laryngectomy in February, 1926. Has resumed practice of medicine.

Fig 202.—Photograph of larynx removed from Case VIII.

treatment, would not now be alive. Many of them have splendid buccal voices and are able to converse over the telephone and carry on ordinary conversation with ease.

These patients were all operated upon by the one-stage operation under rectal anesthesia. The method employed is essentially that described by Gluck and MacKenty.

**Technic of Operation.**—The patient is placed in a recumbent position on the operating table with the head slightly lower than the body. The shoulders are elevated by means of a sand bag,



Fig 203

Fig 203—Case IX Laryngectomy July, 1925 Has a good buccal voice



Fig 204

Fig 204—Photograph of larynx removed from Case IX



Fig 205—Case X Age thirty seven Total laryngectomy in July, 1925

so that the head may be fully extended, thereby bringing the front of the neck into prominence The operator stands on the

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Fig 201—Case VIII. Physician. Age seventy six. Total laryngectomy in February 1926. Has resumed practice of medicine.



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Fig 202—Photograph of larynx removed from Case VIII.

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**Technic of Operation**—The patient is placed in a recumbent position on the operating table with the head slightly lower than the body. The shoulders are elevated by means of a sand bag.

hemostatic forceps. The trachea is now opened by an incision between the first ring of the trachea and the cricoid cartilage extending only half way through the trachea so that a tongue flap of mucous membrane about 1 inch long may be dissected from the posterior and inner surface of the cricoid cartilage. The base of the flap is continuous with the mucous membrane of the trachea. The free end is subsequently stitched to the skin edges for making a better tracheal opening and acts as a barrier to secretion entering the trachea during the convalescent period.

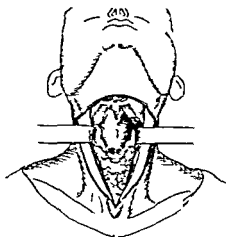


Fig 208

Fig 208—Muscles and soft tissues retracted exposing larynx and thyroid gland

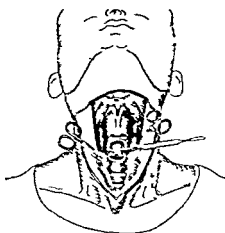


Fig 209

Fig 209—Thyroid isthmus clamped and cut, exposing trachea. Mucous membrane flap dissected from the surface of cricoid cartilage

This of course is omitted if the disease extends as far down as the inner surface of the cricoid cartilage. The larynx is then grasped with a tenaculum forceps, pulled upward and completely severed from the trachea (Fig 210).

A rubber tube is inserted into the trachea as a protection against the insufflation of blood and as an aid to the anesthetist (Fig 211).

The larynx is dissected free from the esophagus from below, upward to a part well behind the arytenoids. It is then returned



to its normal position and an opening is made in the hypopharynx through the thyrohyoid membrane between the hyoid bone and the attachment of the epiglottis. Through this opening the entire buccal cavity is packed with iodoform gauze. If by careful inspection and palpation the growth is found to be entirely intrinsic the larynx should be carefully removed with the view of conserving as much mucous membrane as possible. If there should be evidence of extrinsic involvement the incision should extend well beyond the limits of its involvement even to the

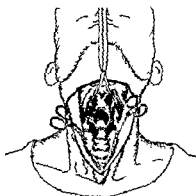


Fig 210

Fig 210—Larynx grasped with tenaculum forceps lifted upward and completely severed from the trachea

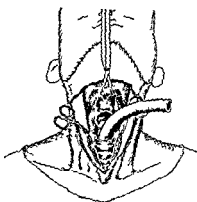


Fig 211

Fig 211—Rubber tube inserted into trachea

extent of removing a large portion of the cervical esophagus lateral wall of the pharynx and base of the tongue. All bleeding vessels should be carefully tied. A Rehfuess feeding tube should be introduced through the most patulous side of the nose to the stomach and the pharyngeal opening closed by two rows of sutures using No 0 catgut (Fig 212).

The tracheal stump is now attached to the skin surface by interrupted silk sutures. To make the union more secure and complete all fat is removed from under the skin edges on both sides and the first ring of the trachea is removed submucously

as suggested by Dr Maishick of Vienna and described to the writer by Dr George G Carroll of Rochester, N Y (Fig 213)

The sternohyoid muscles are sutured together in front of the esophagus. Four open rubber tube drains are introduced: two above, one at the depth of the wound at each corner. Two below, one on each side of the tracheal stump (Fig 214)

The horizontal incision above is completely closed. One mattress suture is placed in the midline incision above, and one just above the tracheal opening. The midportion is left open

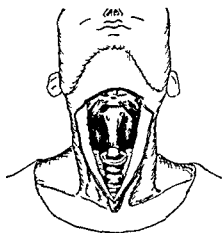


Fig 212

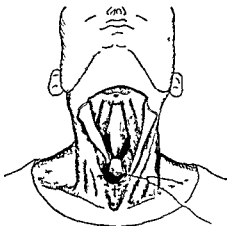


Fig 213

Fig 212 —Larynx completely removed. Pharyngeal opening partially closed

Fig 213 —First ring of trachea removed submucously. Trachea sutured to skin

for drainage and inspection. A No. 8 laryngectomy tube is inserted in the tracheal opening and the wound dressed with moist bichlorid dressings (Fig 215).

*Postoperative Treatment*—A competent nurse, especially trained in the care of laryngectomized patients, should be in constant attendance day and night for the first ten days. Drugs which inhibit the cough reflex should not be given. A substantial well-working suction apparatus should be easily accessible at all times. A short bronchoscope with extra lamps, small battery, and suitable grasping forceps are indispensable when

tongue, part of the pharyngeal wall, esophagus, and lateral structures of the neck. It is possible to remove in such an operation part of the common carotid artery, internal jugular vein, and pneumogastric nerve of one side together with the adjacent structures. If a portion of the pharynx and esophagus is removed, so that it cannot be united over the feeding tube, a permanent pharyngo-esophageal fistula in the neck is made by sewing the mucous membrane to the skin. This is subsequently closed by plastic surgery.

The remaining 2 cases represent an entirely different type of patients, in that the cancer involved the epiglottis, base of tongue and pyriform sinuses without involvement of the larynx. They will also serve to illustrate what can be accomplished in totally extrinsic cancer, which was formerly considered and still is looked upon by some as a hopeless condition.

The first patient is a man fifty four years of age and head of a large manufacturing company who was first seen by me fifteen months ago with a squamous-cell carcinoma involving the epiglottis and base of the tongue. Diagnosis confirmed by biopsy. Under rectal anesthesia a preliminary tracheotomy was performed and approach to the growth was made through the subhyoid region using the radio knife for the entire operation. After the removal of the growth a nasal feeding tube was inserted and the external wound completely closed. He made a satisfactory recovery and is now completely well with no evidence of recurrence.

Next case is a woman, fifty eight years of age, who was admitted to the hospital in April one year ago, with squamous-cell carcinoma involving the epiglottis, base of the tongue and left pyriform sinus. Diagnosis confirmed by biopsy.

A similar procedure was followed in her case, as described in the previous one with the result that after a long convalescence the involved area has entirely healed and her swallowing function good. Four months ago she developed a metastasized gland on the right side which has been controlled at least temporarily by surrounding the gland with radium emanations and the insertion of emanations within the gland. This is the

first patient on whom I performed this operation which proved both interesting and instructive, inasmuch as her stubborn Irish manner taught us that it was unnecessary to keep a nasal feeding tube and tracheotomy tube in place until a swallowing function



Fig 216—Case of carcinoma involving the epiglottis, base of tongue, and left pyriform sinus. Operated on by the subhyoid route in April, 1925. This shows metastasis in the right side of the neck, which has since been entirely controlled by the use of radium emanations.

was thoroughly established. I have performed three such operations, the third patient having a far more extensive involvement, which necessitated the resection of a carotid artery and an internal jugular vein on the left side. He died of bronchial pneumonia ten days following the operation.



## CASES OF CANCER INVOLVING THE LARYNX, TONSIL, AND EAR

I SHALL present some cases of cancer involving the larynx, tonsil, and ear, showing the results of the combined treatment of surgery and irradiation

**Case I**—This patient had carcinoma of the larynx. Diagnosis made by biopsy. The growth was extensive, involving the larynx and the upper end of the esophagus. When she was first seen and at a time when the prognosis was most favorable and growth not so extensive, operation was then refused. Later a tracheotomy became necessary and she was then quite anxious to have the operation performed. The operation was performed five years ago. You will observe that the larynx has been totally removed and also the upper part of the esophagus. The free end of the esophagus was then brought laterally and attached to the skin, this opening you will note on the right side of the neck through which the feeding tube is inserted. This method we have not used since, as experience has taught us that when the esophagus is involved the diseased area is completely removed and the pharyngeal wound is left wide open until sloughing and healing has taken place. The pharyngeal opening is then easily closed by a plastic operation. She has consented to allow us to close this condition within the next few weeks in order that she may be able to swallow her food normally. Irradiation alone has not given us any favorable results whatever in carcinoma of the larynx, but when seen early enough the combined use of surgery and irradiation have given most excellent results.

**Case II**—This patient had squamous-cell epithelioma involving the base of the tongue, the epiglottis, and the lateral wall of the pharynx. She presents the type of case in which it was formally thought that no favorable results could be expected

by treatment of any kind. Her case has been most instructive. The treatment in this patient consisted in a subhyoid pharyngotomy with removal of the diseased area at the base of the tongue, epiglottis and the lateral wall of the pharynx by the use of the radio knife. A tracheotomy was deemed necessary and the patient was fed by means of a nasal feeding tube. Following the operation she was most uncomfortable from the constant drainage of the secretions from the sloughing area into the trachea which was the source of much irritation and annoying cough. As she was unable to swallow fluids by mouth without its entering the trachea after several weeks without any improvement in the swallowing function it was suggested to the patient that we remove the larynx in order that she could properly swallow her food. This she absolutely declined and furthermore stated that she was going to remove the feeding tube and tracheotomy tube and return home. Even though the danger of this was pointed out to her she replied that she would rather be dead than to continue in her present state. She carried out the threat both feeding tube and tracheotomy tube being removed. She returned home and reported to the hospital two weeks later in splendid condition and able to swallow fluids without any difficulty. The experience thus gained has enabled us to treat similar cases with more comfort and better results.

*Case III*—The histories of these patients are all very similar. For varying periods they have been treated medically for laryngitis without a direct inspection of the larynx being made. This patient received similar medical care until she came under the care of Dr. M. Marshall who made the diagnosis and sent her to us for treatment. The larynx was completely removed two years and ten months ago and there has been no evidence of recurrence. She is doing her usual work, feeling fine and is quite cheerful.

*Case IV*—Another case of laryngeal cancer with total removal of the larynx a few months ago. You will note that there is a recurrence in the glands of his neck on the right side.

He is now being treated with irradiation. While the trachea stump and wound are in a healthy condition, yet in this type of recurrence the prognosis is generally most unfavorable.

**Case V**—Another case of extirpation of the larynx. He presents a type of case in which a portion of the esophagus was removed and the pharyngeal wound allowed to remain open until healing had taken place, after which a plastic operation was done to close the pharyngeal wound. He has made a most favorable convalescence. There is no evidence of recurrence and he has gained 20 pounds in weight.

**Case VI**—This one is the youngest patient. He was twenty-nine years of age at the time of operation, which was performed two years ago. He had a most interesting history, which showed that he was treated for asthma and dyspnea until he was seen by Dr. Husik, who at once recognized the condition. A tissue diagnosis was made and he was later referred to us for operation. His convalescence was rather prolonged, for the preoperative treatment by x ray and radium made the operation more difficult. He is now in excellent health, has gained his normal weight and is now driving a sight seeing bus.

We have had 57 cases of carcinoma involving the larynx referred to the radiologic clinic, out of this number only 7 cases were operable. All of the 7 operated upon were treated with irradiation. All are living but 2. 1 died of carcinoma of the stomach and the other was killed in an accident.

**Case VII**—This patient had carcinoma involving the right tonsil, anterior pillar and lateral surface of the tongue. Her history shows that in November 1921 there was a partial removal of the growth by means of a cold snare followed by the treatment of radium and x ray. She was later referred to our clinic and this entire diseased area was treated by the implantation of radium followed by external application of radium plaque. Four years has elapsed since her first treatment and there is no evidence of any recurrence. The scar resulting from the diseased



area looks healthy and the patient is free of symptoms. We have noticed that the tonsil tissues are particularly susceptible to the use of irradiation. It is the treatment of choice and our results have been most encouraging. Carcinoma of the tonsil responds to irradiation far better than the same type of growth in any other part of the nose and throat. We have had two deaths from hemorrhage following the treatment of carcinoma of the tonsil by this method due to deep and extensive sloughing involving some of the larger vessels of the neck. We are now using milder doses and if sloughing becomes very extensive we then ligate the external carotid with the view of lessening the danger from this complication.

**Case VIII**—This patient had carcinoma of the ear which was first seen in 1914. It began as a small pimple involving the skin of the left auricle. This gradually grew in size associated with pain and discomfort. He was then referred to Dr Pancoast who later removed the auricle and surrounding soft tissues by means of the electric current. This was followed by the use of irradiation. He was admitted to this hospital in 1920 because of some discomfort from the middle ear and pain in the region of the mastoid. x Ray examination showed some involvement of the mastoid cells which were subsequently operated upon and at which time the mastoid area was found to be necrotic due to an infection and not an extension of the carcinoma. He has after a stormy convalescence regained his health and is now feeling perfectly well and free of symptoms after eleven years from the time the diagnosis was made.

# CLINIC OF DRS J L WEATHERWAX AND H M SHARP

PHILADELPHIA GENERAL HOSPITAL

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## PHYSICAL CONSIDERATIONS IN THE USE OF RADIUM AND $\alpha$ -RAYS

**1 Physical Aspects of Radium and Its Filtration**—In 1896 Professor Becquerel discovered that uranium gave a radiation of sufficient penetration to affect a photographic plate covered with black paper. Soon thereafter Mme Curie found that the ore pitchblende, from which uranium is obtained, gave forth this radiation much more strongly than uranium itself. She then made a chemical analysis of pitchblende and discovered two new elements, each of which was found to be more strongly radio-active than uranium. These elements she named polonium and radium.

In further experiments it was found that the element radium is unstable, the atoms of radium gradually breaking up into atoms of elements of smaller atomic weight. This is a direct consequence of the radiation, in the process of which an atom of radium of atomic weight 226 loses an alpha particle, of atomic weight 4. The residue of the radium atom is a new atom, of atomic weight 222, called radium emanation. The radium emanation atom in turn breaks up into radium A and radium A goes to radium B and C. This is shown diagrammatically in Fig. 217. It is seen by the diagram that radium C must be produced before beta and gamma radiations are emitted.

Since radium emanation is the first disintegration product of radium, and goes on to give radium C, either radium or radium emanation can be used to obtain beta and gamma radiations. If the radium element is used, some radium salt is sealed in a glass tube and placed in a brass container, which acts as a filter to

remove the soft beta radiation and as a protection to the glass. The element radium is applied to patients in the process of

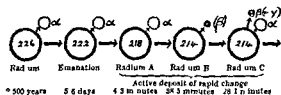


Fig 217 —Atom c disintegrat on of radium

treatment. There is always danger of loss of the radium by carelessness. However the radium salt can be dissolved in a



Fig 218 —Safe conta nng two grams of radium

weak hydrochloric acid solution placed in a safe and attached to an apparatus for collecting the radium emanation as shown

in Fig 218 The radium disintegrates, giving a certain quantity of radium emanation per twenty-four hours As the radium emanation is a gas, we can collect it, purify it, and pump it into small capillary tubes by means of the apparatus shown in Fig. 219.

The application of radium emanation can best be compared with the application of the radium salt by an analogy to the use of water If one is to consume water at its source where a con-

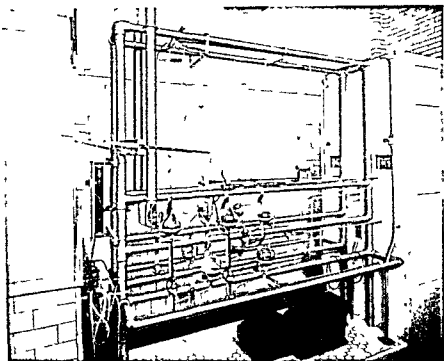


Fig 219—Glass apparatus for collecting radium emanation from the radium in the safe

stant quantity is produced, one does not have to consider the amount consumed. However, if the water is carried to a distance and consumed from a tank, the rate of refilling the tank must be considered in terms of the rate at which the water is consumed. The water, whether used at the source or from the tank, is the same water, and in the same manner the disintegration product radium C is the same, whether it is formed from radium emanation in contact with radium or from radium

emanation in a separate container. If radium emanation is used, its rate of decay must be taken into consideration, while if radium salt is used radium emanation is formed from the radium salt just as rapidly as it changes over into radium A, B, and C. Given a certain number of millicuries of radium emanation, half will have disintegrated to radium A in 3.85 days, but in the same time the same quantity of radium emanation will have been formed from the source radium. A quantity of radium emanation can be pumped from the radium daily, giving a new supply of tubes to be used on patients.

The radium emanation is pumped into capillary tubes of about  $\frac{1}{2}$  mm opening. These tubes are sealed, taken from the apparatus, and divided into tubes 14 mm long. The glass tube is then placed in a small silver tube having a wall  $\frac{1}{2}$  mm in thickness. The silver tube is marked by a definitely colored enamel so as to be able to identify it. For certain uses a smaller capillary tube is employed. A length of about 40 cm is filled with the emanation, sealed, and removed from the apparatus. This long tube is cut up into small tubes 3 mm in length by a gas flame. An attempt is made to have each tube contain about 0.5 to 0.7 of a millicurie of emanation. The large tubes when applied to patients are contained in small silver tubes, while the small emanation tubes are placed in needles and inserted directly into the tissue so that bare glass is in direct contact with the tissue. To distinguish the tubes the large emanation tubes are designated "silver tubes" and the small tubes are called "bare tubes."

These capillary tubes of radium emanation are standardized by comparing their rate of discharge of an electroscope to the discharge of the same electroscope by a radium standard of 25 mg, as shown in Fig. 220. All of the bare tubes are standardized as a group and the total number of millicuries obtained. With an apparatus as shown in Fig. 221, consisting of a sensitive galvanometer connected to a large ionization chamber, the relative value of each bare tube is ascertained.

A record is made of the number of millicuries and the date of standardization for silver tubes and bare tubes. This record

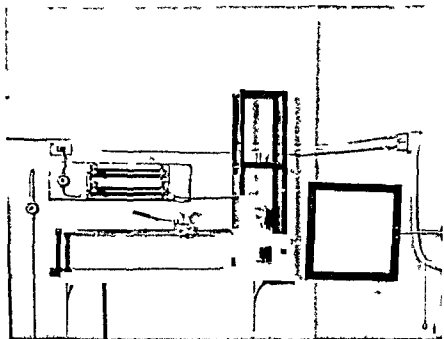


Fig 220 —Electroscopic system for standardizing emanation tubes

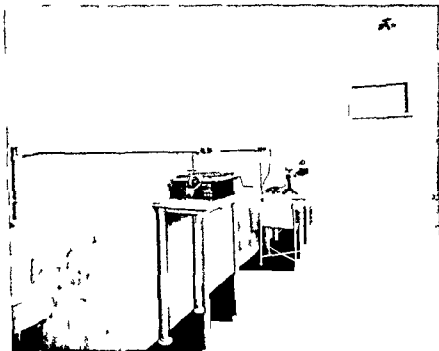


Fig 221 —Ionization chamber and galvanometer for measuring the strength of emanation tubes for implantation

is corrected every twenty four hours or less for the decay of the radium emanation

The alpha rays have very little penetrating power and are stopped by the walls of the glass tube. The beta and gamma rays emerge from the glass and are the rays used in radiation therapy. If only gamma rays are desired the beta rays can be stopped by the  $\frac{1}{2}$  mm of silver and an additional 2 mm of brass.

**2 Application of Physical Measurements of x Ray Therapy**  
—Physical measurements of Roentgen radiation can be of service to the roentgenologist in aiding him to deliver a definite x ray intensity of known penetration into a tumor. This can be accomplished in the following manner (1) standardization of

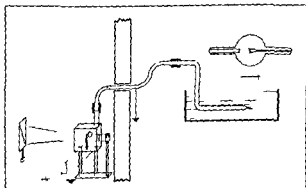


Fig 222 —Electroscopic system for standardizing x ray machine and measuring penetration

x ray installations (2) the application of depth dosage charts to individual patients and (3) the use of some method of measuring the output of radiation during treatment

1 The standardization of an x ray installation is made for the purpose of knowing the output of radiation. The method in use by us in making these standardization measurements is an electroscopic system attached to a horn ionization chamber<sup>2</sup> as shown in Fig 222. The horn ionization chamber has a capacity of about 1 c c. A water phantom contained in a vessel of aluminum with  $\frac{1}{4}$  inch of soft rubber vulcanized on the inside is used to represent the patient. The size of the water phantom is made to compare in size to the average patient.

The procedure in making standardization measurements is to employ the same factors in operating an x ray machine from one installation to another which are as follows 200 kv 4 ma 0.51 mm of copper and 1 mm of aluminum as filters a field 20 cm in diameter and 50 cm skin target distance With the x ray machine in operation a measurement representing the output of radiation is first made with the ionization chamber half submerged in water The operator stops the x ray machine and a known quantity of radium is then placed in a fixed position over the electroscope A reading of the ionization current produced by the radium radiation is obtained The value of the ionization current for the radium is divided by the number of milligrams of radium The ionization current representing the x ray intensity is divided by the ionization current representing 1 mg of radium intensity giving the number of milligrams of radium to produce the same intensity as the x rays From our experience we know that 500 mg of radium represents the output of radiation for a good x ray installation as measured by our apparatus If the intensity from an x ray installation gives an equivalent intensity of less than 500 mg of radium we are quite sure that we are not getting the output of radiation that we should We have measured the intensity of x ray installations giving an equivalent radium intensity of 350 mg which means that there is 30 per cent loss in intensity

If the x ray installation gives an output of radiation which has an equivalent radium intensity below 500 mg it is essential that a careful examination be made of all the parts entering into the operation of the x ray machine A low output of radiation does not necessarily mean that the x ray machine is at fault but may be due to a leaky insulator a milliampere meter reading too low or other factors entering into the adjustments of the x ray installation When adjustments and changes in the installation are made each one should be followed by measurements of the output of radiation so as to determine whether there has been an increase or decrease In practically all installations the output of radiation can be brought up to the normal constant of an equivalent radium intensity of 500 mg if the manufacturer



and the physicist will work together to eliminate the losses. The physicist has not done his full duty in simply reporting a low intensity but should try to find and help to eliminate the cause.

If the  $x$  ray installation gives an equivalent radium intensity of 500 mg we can compute the number of milliamperere minutes to give an erythema at one exposure. With the same voltage milliamperage filter field and skin target distance an erythema of equal intensity will be obtained in the same number of milliamperere minutes by other standardized  $x$  ray installations. Roentgenologists from various parts of the country can compare their erythema intensity when working with standardized  $x$  ray installations.

2 We should have a knowledge of the average wave length as well as the intensity of the  $x$  rays. The average wave-length delivered by an  $x$  ray installation governs the penetration of the  $x$  rays in the tissue. We have measured the penetration in water for  $x$  rays of a definite average wave length so that if penetration measurements of an  $x$  ray installation check our penetration measurements for the same depth in water and for the same field we know that we must be dealing with the same average wave length.

Ionization measurements of the  $x$  ray intensity on the surface of the water are made with the ionization chamber half submerged in water. The ionization chamber is lowered into the water and ionization measurements made of the intensity at various depths as shown in Fig. 221. The  $x$  ray intensities at the various depths are compared with the  $x$  ray intensity on the surface of the water and the percentage of  $x$  ray penetration computed. These percentage intensities are then compared with depth dosage charts made on an  $x$  ray installation under similar conditions and giving the same average wave length. If there is a close agreement of the penetration intensities and there should be with the same average wave length then the roentgenologist can safely use the depth dosage routinely while treating patients. It is obvious that the time to get depth dosage charts of each  $x$  ray machine standardized would run into weeks so we compare the measurements of a few penetration

percentages to those on the charts and assume that there is a close agreement for other points in the field. There are quite a

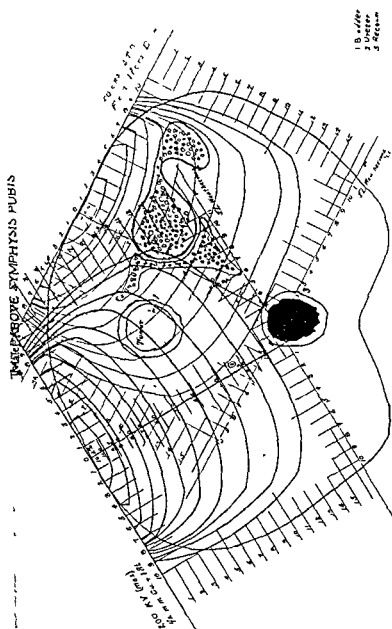


Fig 223—Anatomical cross section chart showing the area to be treated and the method of using penetration charts to determine the most efficient arrangement in cross firing

few different sets of curves needed to outline the distribution of  $\alpha$ -ray intensities in the use of any given installation, such as are found in varying the voltage, the size of the field, the filter, and

the skin target distance. Of course the roentgenologist will tend toward a comparatively few standard combinations in running his x ray machine but these combinations vary from one roentgenologist to another.

These charts showing the penetration of x rays can be used as a guide in the treatment of patients, as shown in Figs 223 224 and described in detail in a recent publication.<sup>3</sup>

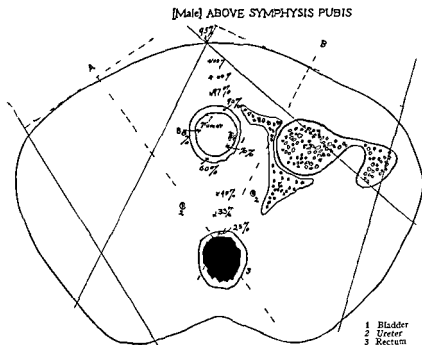


Fig 224—Anatomical cross-section of the tumor with location and direction of fields to be used as a guide in treatment

3 Even though an x ray machine has been standardized and from time to time restandardized there are a great many advantages in having an ionization chamber in a fixed position between the patient and the copper filter, so as to have a continuous reading of the output of radiation while treating patients.<sup>4</sup> With an ionization chamber in the field of radiation during treatment of patients we are measuring the output of radiation as well as measuring the input of electrical energy

The ionization chamber is made of aluminum plates of a total thickness of 1 mm, which takes the place of the usual 1 mm. of aluminum filter. Figure 225 shows the ionization chamber before being mounted between the copper filter and the patient. The ionization chamber after being mounted is connected to a galvanometer and to 300 volts of radio B-batteries. The galvanometer and scale are mounted in the booth with the

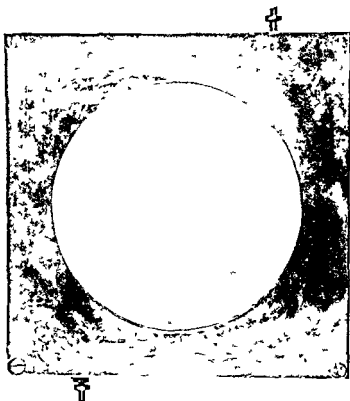


Fig 225 — Ionization chamber attached to the x ray tube holder for measuring the output of radiation during treatment

control stand where the operator can easily observe the readings, as shown in Fig 226

The operator will have more respect for careful work if he can see the effect caused by fluctuations in voltage and milliamperage on the output of radiation. The omission of a filter will be observed within a few seconds after starting the x-ray machine because of the increased galvanometer reading produced by the increased output of radiation. A more detailed treatment of this method is found in a previous publication <sup>4</sup>

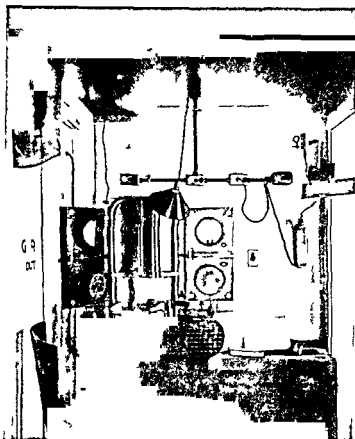


Fig 226—Scale for recording the ionization measurements of radiation intensity shown in operator's booth

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### GASTROSTOMY FOR CANCER OF THE ESOPHAGUS

NINETY patients with carcinoma of the esophagus have been treated in the Radiologic Department since it was organized in



Fig 227.—Complete obstruction at the level of the third to fourth thoracic vertebrae

1922. Eighty-four patients were males and 6 females. Tobacco, alcohol, and coarse foods have been blamed for the predominance

in the male In none of our patients was there a history of the swallowing of corrosive liquids The youngest was thirty-nine; 12 were between forty and fifty, 29 between fifty-one and sixty; 38 between sixty-one and seventy, 9 between seventy-one and eighty; and the oldest was eighty-five years of age To summarize: Cancer of the esophagus is not a rare condition. It may occur at any point in the esophagus, but we have found it most



Fig 228 —Complete obstruction at level of the seventh to eighth thoracic vertebrae

commonly at the levels of the fourth (Fig 227) and the seventh (Figs. 228, 229) thoracic vertebrae

Apparently the cancer had to be present sufficiently long to produce an obstruction before any subjective symptoms were noticed The first symptom dysphagia, occurred abruptly, so that all our patients were explicit as to the date of onset Their first difficulty was commonly described as a "sticking in the

throat" of an imperfectly chewed piece of meat. The bolus was usually regurgitated, but often it was forced onward by drinking a glass of water. Solid foods passed with increasing dysphagia during the first two or three weeks, and then the heavier semisolids caused difficulty during the next month. After this, soups and gruels could be tolerated for an average of another three or four months and ice cream somewhat longer.



Fig 229 —Obstruction is not complete but is situated at the same level as Fig 228.

Thereafter water caused difficulty, and in a few instances the obstruction was complete when the patient first came to the hospital. The rapid progression of symptoms is always strongly suggestive of cancer. In several instances the interval between the onset of dysphagia for solid foods and inability to swallow any food was only two to three months, and the longest interval was, in one case, ten months.



A feeling of fulness or compression behind the sternum during ingestion of food was frequently noted but actual pain was never mentioned. Loss of weight occurred early was progressive and was mainly due to starvation and later to dehydration rather than to the cancer itself.

The diagnosis is established by the *x* ray and the esophagoscope. The latter should never be used before eliminating the possible presence of an aortic aneurysm which might be ruptured during the passage of the instrument. Fluoroscopy and skia grams will reveal aneurysm and other extrinsic causes of obstruction as well as such intrinsic lesions as cardiospasm and diverticula. The barium in buttermilk mixture is impeded or arrested by late cancer but may pass through an early cancer without any signs visible through the fluoroscope. An early lesion may be manifested by delay in the passage of a barium mashed potato mixture but in any patient complaining of dysphagia a negative diagnosis must never be made unless a 10 grain sized capsule filled with barium or bismuth passes without delay. The fluoroscope will reveal the presence and the level of the obstruction but often without determination of its nature. The extent and outline of the lesion can only be shown satisfactorily by *x* ray by filling the entire length of the esophagus with barium. Lesions of the upper fourth are best shown when the patient is in the erect posture. The special technic advocated by Manges has proved the most satisfactory for the lower three fourths. He requires the patient to lie prone with the right arm extended alongside the body the left arm flexed at the elbow and drawn up so that the patient rests on the elbow when rotating the body toward the right. The left knee is flexed and the entire body inclines a little toward the right keeping the spinal column as nearly straight as possible. This position is called by Manges right oblique prone. It makes possible the entire filling of the esophagus because the cardiac end is higher than the upper fourth and prevents the rapid emptying into the stomach of the opaque mixture. Absolute verification that the lesion shown by the roentgenologic examination is cancer can be obtained only by esophagoscopy with removal of a biopsy.

Cancer of the cervical portion of the esophagus should be excised. Resection of the thoracic esophagus with its high operative mortality and paucity of cures has never been attempted in this hospital. We have employed intra-esophageal applications of radium and deep x ray therapy but without noteworthy benefit. Some of the ulcerative cases treated by radium were apparently healed on their mucosa aspect but this did not check the deeper growth or prevent pulmonary infection, which is the usual cause of death in esophageal cancer. We have under consideration a new, and as yet untried, technic for using radium which we hope may give better results.

In the meantime, gastrostomy is our best means for prolonging the life and comfort of these patients. In our early cases we employed the Senn<sup>2</sup> type of gastrostomy because of its simplicity. It proved satisfactory while the patients were under direct control within the hospital. Following any form of gastrostomy the inflammatory process complicating the cancer subsides, with a corresponding return of the ability to swallow. We soon found that the patients who went home began taking all nourishment by mouth, and permitted their gastric fistula to close by their failure to retain the gastrostomy tube. With recurrence of severe dysphagia a second gastrostomy had to be performed. The same objections hold good with all forms of gastrostomy, including the Witzel,<sup>3</sup> which are not provided with a tract lined by a mucous membrane.

The Ssabanajew-Franck<sup>4</sup> gastrostomy provided a mucous tract by drawing a long funnel of stomach obliquely out through the abdominal wall. It is open to two serious objections. The stomach rapidly shrinks in size when esophageal obstruction prevents its normal filling. The creation of a long funnel from a small stomach exerts a painful drag on the gastrophrenic ligament. The continued weight of a full stomach drags the funnel downward, so that the constrictor effect of the external oblique muscle against the rib margin is lost, and the stomach contents leak.

We have come to rely upon the Janeway<sup>5</sup> gastrostomy and I will now demonstrate its performance to you on this white man,

aged sixty three years. He gives a history of dysphagia beginning four months ago June 1926 and is able to swallow liquids only. His radiologic examination was negative for any intrathoracic lesion except the esophageal obstruction shown by these skiagrams (Figs 230-231). Fluoroscopy with liquid barium shows esophageal obstruction starting at the level of the fourth thoracic vertebra and extending almost to the eighth thoracic



Fig. 230. The obstruction is not complete. The lesion starts at the level of the fourth and continues to the eighth thoracic vertebrae.

vertebra. No metastasis to lungs is demonstrable. Biopsy obtained through the esophagoscope shows a squamous cell carcinoma. Wassermann is negative, blood urea 23, blood uric acid 4.4. He has lost 45 pounds in weight since June and is becoming dehydrated. His heart shows an aortic insufficiency and râles are heard at the base of the right lung.

The patient was given our usual preoperative medication for local anesthesia, consisting of morphin and magnesium sulphate.

as advised by Gwathmey. We use local anesthesia routinely because of its simplicity and lack of shock to a weakened patient. A  $\frac{1}{2}$  per cent. solution of novocain infiltrated in a line starting 2 cm. below the tip of the left twelfth rib, and paralleling the left costal cartilages, to the ensiform, blocks the left intercostal nerves supplying the operative site. An infiltration from the ensiform to the umbilicus in the midline of the abdomen blocks all the



Fig. 231—Same case as Fig. 230. Barium filled capsule is lodged at the upper end of the obstruction.

*small nerve-fibers that cross from the right side.* Directly under the proposed longitudinal line of incision through the upper left rectus we infiltrate the peritoneum and posterior sheath of the rectus (Fig. 232). Complete anesthesia and fair muscular relaxation is obtained in from six to ten minutes.

We will make a 5 cm. incision through the inner third of the upper left rectus, starting about 2 cm. from the costal border.

The peritoneum appears to be well injected with our novocain solution and incision through this is painless. The anesthesia will permit of a limited palpation of the liver, but if a more

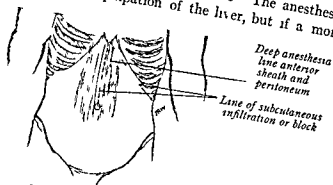


Fig 232 —Lines of anesthesia.

extended examination is found advisable, several minutes of gas anesthesia may be used. This liver is slightly enlarged, its edges are sharp, its surface smooth and it shows no indications of being

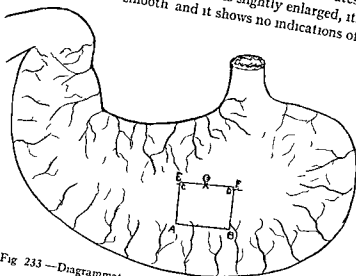


Fig 233 —Diagrammatic explanation of stomach incision

the seat of metastasis. We have never found metastatic nodules in the liver at the time of operation in a case of esophageal cancer.

The stomach is not supplied with pain sensory nerves, hence local anesthesia of it is unnecessary. By gentle traction we deliver through the incision a relatively avascular area of the anterior stomach wall, near the cardiac end. Four points (*A*, *B*, *C*, and *D* of Figs 233, 234) on the anterior stomach wall are grasped by Allis forceps, which will outline a rectangular

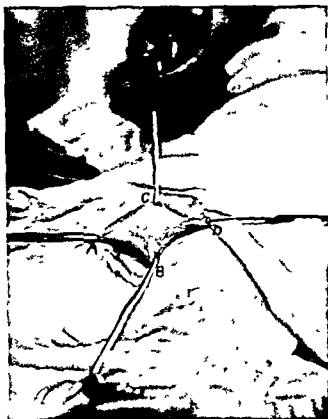


Fig 234—Rectangular section of anterior stomach wall delivered and ready for incision

area measuring 2.5 x 3 cm. The sides (*A-B* and *C-D*) measuring 3 cm. parallel the curvatures of the stomach. Throughout the entire operation, we use gauze pads to prevent contact between the gastric mucosa and the abdominal wound. We incise three sides of the square through all the gastric coats leaving the base line (*A-B*) intact (Fig 235). Turning down the flap (*C-D*) we have a square opening in the anterior stomach wall with its

base at *A B* and its upper margin at *E F* (Fig 236). An Allis forceps is applied to the midpoint (*G*) of the upper incised margin (*E F*). A No 16 rubber tube is laid in the stomach running in the midline of the flap on its mucous surface (Fig 237) and lightly secured with a chromic catgut suture. Gentle traction upward at point *G* causes the corners *E* and *F* to straighten out and disappear. The Allis forceps on *C D* and *A B* are

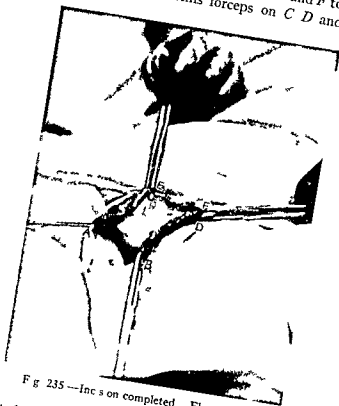


Fig 235—Incision completed. Flap *in situ*.

approximated to fold the gastric flap around the rubber tube. The straight line thus formed is closed by inversion sutures and buried by a second suture line thereby closing the stomach and forming a mucous-lined serous coated tube (Fig 238). After reduction of the stomach and tube into the abdomen we determine the position which the tube naturally assumes in relation to the anterior parietes and then at a point 15 cm above that

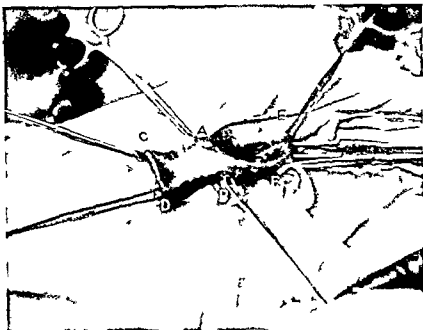


Fig 236 —Flap turned down exposing mucosa

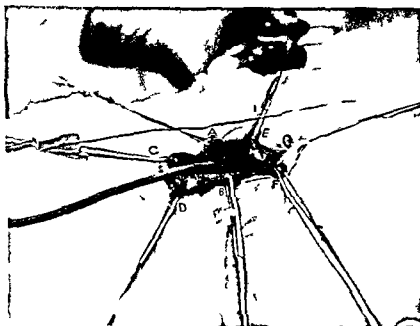


Fig 237 —Gentle traction applied at midpoint G of the base line E F

level we make a stab wound through the outer third of the rectus muscle. The rubber tube and its surrounding gastric tube are



The specimen from which the following report was made contained 20 c c of blood-stained fluid which was mixed with mucus and detritus. It was cleared by centrifugation. Free HCl—none Total HCl—40

Dilution of material	1	4	8	16	32	64	128	256	512	1024	2048	Control
Pepsin	+	+	+	+	+	+	+	+	+	+	+	—
Rennin	+	+	+	+	+	+	+	—	—	—	—	—
Pancreatic amylase	+	+	+	+	+	+	+	+	+	+	+	—
Pancreatic protease	—	—	—	—	—	—	—	—	—	—	—	—
Pancreatic lipase	—	—	—	—	—	—	—	—	—	—	—	—

Fig 240

In this specimen pancreatic amylase is present. Apparently we have a regurgitation through the pylorus.

*Specimen contained about 8 c c of turbid yellowish fluid It contained detritus, no blood, and no bile.*  
 Cleared by filtration Free HCl—none Total HCl—80

Dilution of material	1-4	8	16	32	64	128	256	512	1024	2048	Control
Pepsin	+++	+++	+++	+++	+++	+++	+++	+++	+++	+	-
Rennin	+++	+++	+++	+++	+++	+	-	-	-	-	-
Pancreatic amylase	-	-	-	-	-	-	-	-	-	-	-
Pancreatic protease	-	-	-	-	-	-	-	-	-	-	-
Pancreatic lipase	-	-	-	-	-	-	-	-	-	-	-

Fig 241

**Results** From the above tabulation it appears very evident that in this sample (Fig 241) there had been no regurgitation through the pylorus, since there is complete absence of the pancreatic enzymes, and there is also an absence of bile in the sample Both the gastric enzymes appear quite active.

Gastrostomy should be performed as soon as the diagnosis of cancer of the esophagus is made. When performed early the operative mortality should be nil. Gastrostomy prevents starvation and prolongs life. Immediately after gastrostomy the patient should abstain from all food by mouth, but should swallow sterile water freely to irrigate the esophagus and its contained ulcer. Food is given slowly. Water only is given during the first thirty six hours after operation. During the following twenty four hours 1 ounce of one quarter strength formula at two hour intervals is given through the gastrostomy tube. After using various formulas we have found this one to be satisfactory.

	Ounces
Pepton $\pi$ 1 milk	50
Oat meal gruel	16
Cream	3
Olive oil	2
Butter	2
Sugar	3
Four eggs	

Divide into five feedings—9 and 11 A. M. 1 P. M. and 5 P. M.

Juice of one orange per day

After each feeding give 3 ounces of water through the gastrostomy tube.

If the patient stands the one quarter strength well for the next twenty four hours the amount of feeding is doubled making 2 ounces every second hour. The following twenty four hours one half strength is used and so graduated up to the full strength formula and its routine administration. The condition of the patient regulates the rapidity of advancement to full formula. Water at all times is given freely by mouth. The formula is always given by the gastrostomy tube. There soon results an absorption of the inflammatory exudate around the ulcer with a return of the ability to swallow. The patient is then prone to discard his gastrostomy tube and resume taking all food by mouth. Under these conditions the Janeway gastrostomy will remain patulous indefinitely whereas the temporary gastrostomies of the Senn and Witzel types will close up completely.

After the first few days the gastrostomy tube may be inserted only during each feeding, or it may be retained between feedings.

provided it is changed every few days. An ordinary rubber bulbed glass medicine dropper inserted into the end of the gastrostomy tube is the best means for closing it between feedings. In our experience there is far less leakage of gastric contents after the Janeway operation than after the other forms of gastrostomy.

The immediate operative mortality of gastrostomy for esophageal cancer is high because operation is so commonly deferred until patients are starved and dehydrated. We very commonly have withheld operation for one or two days in an effort to overcome extreme dehydration.

Of our 26 gastrostomies, only 1 was a female. Eighteen died within the first three months after operation and 5 in the next succeeding three months. Three are still living, 1 is doing well after one month, 1 eight, and 1 ten months respectively after operation. This record is about the average reported by other surgical clinics. Life would be more prolonged by earlier operations.

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## IRRADIATION THERAPY WITH FRACTIONAL DOSES OF x-RAYS

GENTLEMEN For centuries mankind has vainly sought the cause of, and the cure for cancer. Many theories have been advanced as to the etiology, but none has survived the close scientific scrutiny to which each has been subjected. Only a little better success has attended the efforts to find a cure. These efforts have been directed (a) to completely removing the malignant tissue (the knife), (b) to burning it out (the cautery), (c) to starving it (diets), (d) to poisoning it (colloidal copper, lead etc) (e) to drying it up or "cooking" it *in situ* (electrothermic methods), (f) or to devitalizing the individual cancer cells (irradiation). Vaccines and serums have also been used but with very indifferent results.

The knife, the cautery, and the electrothermic methods can all claim a large number of cures where the diseased tissue has been localized and has not involved a vital organ.

Unfortunately however, only a comparatively small percent age of cases of malignant disease conform to these requirements.

These methods are by themselves quite inadequate when dealing with the more malignant types involving the deeper tissues and with metastases already in the surrounding tissues or even in more distant parts of the body.

It was in the treatment of such cases that so much hope was placed in irradiation therapy for it was thought that here was a method by which the deeply lying malignant cells could be reached.

At first, however, only the superficial tissues could be treated, as the apparatus then available could not produce rays of sufficient penetration to reach the deeply lying organs. Nor was

there any method known for measuring the x ray energy emitted from the tube Under the circumstances only small doses could be given with safety but these were repeated at short intervals of time until a definite superficial reaction was obtained This was known as a skin erythema dose By keeping up this effect for a short time (several days to a week or more) some excellent results were obtained In course of time however it was observed that very frequently the skin and superficial tissues which had been so treated lost their elasticity and became hard and dry This was sometimes followed by sloughing and by the formation of indolent ulcers As deeply lying neoplasms were found to be unaffected it was realized that to reach these without damage to the overlying tissues most of the softer rays must be removed before reaching the skin This was accomplished by using filters of leather aluminium or glass

Carrying out the common belief that only complete destruction of the neoplasm could offer a hope of curing the malady more powerful and penetrating radiations were sought Apparatus was increased in size tubes were designed to give a greater output of energy and the lethal dose technic was promulgated Every effort was made to kill all the cancer cells to cause an endarteritis in the neighboring vessels (and by so doing starve the malignant tissue) and to induce a fibrosis in the surrounding healthy tissue with the hope of walling in the danger zone In theory this heroic treatment had some justification but in practice it was found that what was intended as a knock out blow to the malignant cells proved in many cases to be such to the patient Experience has demonstrated that no matter how intense the irradiation not all the cancer cells are killed that the endarteritis while perhaps starving the cancer cells also starves the normal surrounding cells which may be essential to the well being of the patient and that the enveloping fibrosis is after all a replacement fibrosis of tissue (normal as well as pathologic) damaged by the irradiation and which consequently often involves tissue vital to the existence of the individual This sledge hammer technic has therefore been abandoned by most radiologists and more or less modified by all

The conviction has been gradually growing in the minds of many observers that there is present, in most individuals, some form of resistance to this disease. This seems a logical presumption in view of our knowledge of the powers of resistance possessed by the body to other forms of foreign invasion. It would seem to be justified, also, by cases, even though but few have been reported, of spontaneous cures; and by the finding of scirrhus carcinomata which are regarded by some as evidence of Nature's attempts to cure by "replacement fibrosis," differing from man's attempts, however, in that only the diseased tissue is replaced. Likewise, the presence of a round-cell infiltration in the zone of proliferation of an uninfected malignancy, before any therapeutic treatment has been given, proves that there is an undeniable interaction of neoplasm and stroma.

The preservation of vital tissue in the periphery of a malignant tumor is therefore a matter of great importance.

Ideal therapy, according to Ewing, "seems to require a nice adjustment of relations between a destructive effect on the tumor cells and stimulation of the stroma cells."

"The presence of a round-cell infiltration about a malignancy, whether it occurs as a part of the natural body resistance (Broders) or whether it is stimulated by radiation, is one of the first steps in causing the retrogression of neoplastic elements" (Withers and Ranson). The changes in a tumor after irradiation should be "essentially the same as appear in any malignant tumor of some time of standing, as the result of spontaneous regressive metamorphosis" (Kolischer).

Ewing, in describing the changes which have been observed to occur in a superficial neoplasm while being treated with small doses of irradiation over a period of weeks, resulting in its ultimate disappearance, says, "Exactly what has been done no one knows, but he (the radiologist) has not killed any cancer cells. Sections taken at intervals throughout the tissue so treated show hyperchromation of nuclei and hydropic swelling of tumor cell bodies followed by gradual atrophy of the cells. At the same time the surrounding tissue becomes active, leukocytes emigrate, lymphocytes and plasma cells appear, capillaries proliferate, and



all these invade and replace the tumor mass. A slow regressive process with degeneration of the tumor cells and a progressive process with exudation and proliferation of normal tissue are set going and as a result of these processes the tumor is cured." Similar changes have been observed following the irradiation of tumors lying in the deeper tissues. It appears probable that the reaction of the tissues is an essential process.

The basis of irradiation therapy has been that tumor tissue is more susceptible and more easily destroyed than normal tissue. This is explained by the fact that all young cells particularly those in active process of division which are present in large numbers in neoplastic tissue are more readily affected by the rays than are the more mature cells of the surrounding tissues. But it is also possible to explain it as an increased stimulation of the protective mechanism of the normal tissues. For example, Edsall and Pemberton have concluded that enzymes liberated from the tissue cells by radiation stimulation and circulating in the tissues are responsible for some of the remote effects following irradiation treatment.

Ewing too says "There is reason to believe that cell constituents are ionized and intracellular ferments activated."

According to Piergrossi the action of the irradiation is chiefly if not exclusively on the nuclear chromatin of the tumor cell and not on its stroma. The irradiation ought to continue during an entire period of mitosis so as to act on the nuclear chromatin during the whole time that it is involved in division. According to this theory irradiation should always be prolonged and in fractional doses as small repeated doses act more intensely on the life of the cell than a large dose given in a short time.

Our knowledge of the effects of the rays in the individual cells is still very vague. We do not know whether it is physical or chemical. It probably occurs through ionization produced by the electrons which are emitted throughout the mass of a substance as far as the rays penetrate. The bombardment of the atomic structure of the cell protoplasm produces a rearrangement of the atomic electrons in other words a chemical process, and this in turn to a biologic reaction, and histologic change.

Certain of the chemical substances formed appear to act in the manner of antibodies. Contamin has shown that the inoculation of mouse or rat tumors feebly irradiated produces an immunity against additional grafts of neoplastic tissue. If the dose is too large, inoculation of the irradiated tumor is no longer capable of conferring immunity (Russ).

R. S. Lillie has recently suggested that what we mean by the sensitivity of this tissue or that to radiations is that we can disturb the valence, or combination electrons, of the molecules in those tissues by irradiation. If we can so disturb valency electrons in pathologic tissue that they will tend to resume their former non-pathologic relations then we are accomplishing therapeutic results (Stokes). According to Butts the negative electrons (secondary rays) are responsible for biologic cell change, and these by neutralizing the excess potential within the tumor cells bring about their desired and self-possessed therapeutic action, by repeated small doses of screened radiations rather than the large continuous doses heretofore employed.

Some two years ago, owing to personal experiences and the reported observations of others, one of us (Morgan) made a radical change in the technic he had previously been using. Instead of trying only to kill cancer cells an attempt was made to find a dose (physiologic) which would depress the more easily affected malignant cells while at the same time preserve and stimulate the normal surrounding cells, producing (if such exist) intracellular ferments and antibodies in the blood. Therefore, instead of heavy knock-out doses, small, frequently repeated treatments were used, with highly penetrating, heavily filtered, rays. The biologic action of the penetrating primary beam is comparatively small, their chief value being their penetrability and their power of exciting secondary or negative rays in the tissues.

As the amount of ionization produced within the tissues is a function of the absorption and scattering coefficients, and as it is these secondary (scattered) rays which have the greatest effect in the tissues, large ports of entry were adopted in all cases. The danger to the skin, when using small fractional

doses from the overlapping of these portals of entry is practically nil. The factors used are 200 K.V. 5 m.a. 50 cm. distance filters 0.5 mm Cu and 1 mm Al. portal 200 sq cm. Neoplasms lying within 10 cm. of the surface receive three minutes twice daily or five minutes daily if two visits are impracticable. More deeply lying neoplasms are given ten minutes twice daily the first from one direction the second from the opposite direction.

Cross-firing is employed in order to irradiate the tumor and surrounding tissues equally from all sides.

Among the advantages offered by this technic are the following: the dangers from overdose (either from carelessness of the operator or idiosyncrasy of the patient) are reduced to a minimum; radiation sickness does not occur; fatigue and the discomforts of long treatments are not experienced; systemic shock is absent; and danger of injuring the skin from the overlapping of portals of entry is eliminated.

This technic has been used in a series of cases of various types during the past two years. Not every case has responded as well as had been hoped, but the results have on the whole been most encouraging and in several even quite astonishing. It has seemed that the most surprising results were obtained in the treatment of cases which had previously proved to be unaffected by heavy doses. At the present time a series of cases are under observation at this hospital. Several of these will be demonstrated today.

**Case I—T. C. Male White Age forty nine** Twelve years ago he had sulphuric acid splashed on the skin near the inner canthus of left eye. Six years later a small ulcer developed in this region and persisted in spite of local treatment. Two and a half years ago this was excised together with the lacrimal duct. The wound refused to heal. He was sent to this hospital on January 26 1926. At that time there was a small cavity (about 4 mm. across by 6 mm. in depth) surrounded by indurated tissue which caused a narrowing of the palpebral fissure. Scar tissue was present over the bridge of the nose and eyelid. There was a yellowish discharge.

A diagnosis of basal carcinoma was made. On January 28th treatment consisting of ninety millicurie hours radon was given, two silver tubes being placed in contact with the tissues. This was repeated on February 11th. As no improvement resulted, fractional  $\alpha$  radiation was begun on March 2d. He received fourteen treatments of five minutes each during the next three weeks. Two weeks later, in April, he was given twelve more similar treatments on successive days. The ulcer was entirely healed at the end of the first three weeks' treatment, and the condition has continued to improve since. On April 22d palpation showed the presence of some induration under the upper



Fig 242—Case I

border of the left orbit, but it was difficult to say whether this was disease or scar tissue. Improvement has continued.

Case II.—O S, male, white, age forty-seven. In July, 1925 he noticed a lump on his left cheek. In November, as this had increased in size and other lumps had appeared in the sub-maxillary region, the patient came to the hospital for treatment. Biopsy was done, and a report of round-cell sarcoma made. He was given two  $\alpha$ -ray treatments of five minutes each, but failed to report for more as the growth became so much smaller. He reported again on January 6, 1926, at which time he had a

flattened globular mass about the diameter of a fifty cent piece and a  $\frac{1}{4}$  inch in thickness in the left cheek. There was also an area of induration in the submaxillary region where ulceration had occurred. He was given two treatments of five minutes each on January 6th 7th 8th 12th 13th 14th 15th and 19th. At this time the lesions on the cheek and chin had entirely gone. On February 16th an indurated area about 1 inch in diameter was found in the left supraclavicular space. This received similar treatments on February 16th 17th and 18th. When he reported again on March 8th this induration had disappeared.



F g 243 —Case II

He received daily treatments of five minutes each over all of these areas on March 8th 13th and 17th as a precautionary measure. On April 17th there was no indication of disease in any of these areas.

**Case III** — J C male white age forty eight. In August 1924 he noticed a lump the size of a pea on the left side of his face. It grew rapidly larger. The tumor was removed by operation in December. It grew rapidly again during the next three months. In April 1925 he came to Philadelphia where he received twenty five (so he says) x ray treatments (saturation method). The mass broke down in the center and continued

to grow larger. On admission to this hospital, early in December, 1925, in the left parotid region there was a hard mass  $3\frac{1}{2}$  inches in diameter and purplish-red in color with dilated veins over the surface. The upper part was fixed. There was no involvement inside of the mouth or of the glands of the neck.

The lungs were clear. Clinical diagnosis: Carcinoma of parotid gland.

Starting on December 9th and during the next twenty-one days he was given twenty-two treatments of five minutes each. The mass decreased in size, softened, and broke down on Decem-

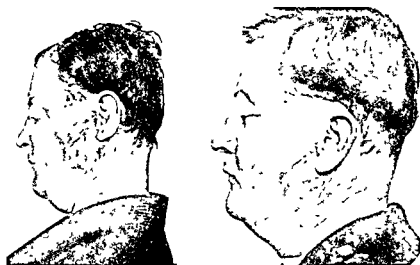


Fig 244 —Case III

ber 18th, discharging freely. Two days after starting treatment all pain had disappeared.

He received further treatments on February 26th and 27th, and again on March 1st, 2d, 8th, 9th, 12th, 13th, and 16th.

He was discharged from the hospital on February 27th and told to report daily, but his attendance became very irregular.

On February 20th, 90 per cent. of the tumor had disappeared. He showed further improvement on May 27th, but has not reported for further examination since that time.



## CLINIC OF DR HENRY K PANCOAST

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### TREATMENT OF CANCER BY IRRADIATION METHODS

THERE are several generally recognized methods of dealing with cancer at the present time. No one of them is adapted to the treatment of every case and the individual who attempts to treat each case by the same procedure is narrow minded and does not have the best interests of his patients at heart. The most important methods now in use are surgery,  $x$  rays and radium and the destruction of tissue containing large masses of cancer cells by electrodesiccation. Other methods such as the injections of certain metallic elements like lead and various sera are passing through periods of trial in the search of a specific cure for inaccessible or generalized cancer. When the plan of attack is being formulated in the case of any malignant growth we should consider every possible means of dealing with the condition, and then select the one or more methods best adapted to meet the situation. As our present talk deals specifically with irradiation therapy, the discussion of cancer treatment will be limited to the use of  $x$  rays and radium, and the other methods will be mentioned only by way of comparison of results or as they may be advantageously combined with irradiation.

It is not possible to discuss the irradiation treatment of cancer in a general way for the reason that the disease differs in its type and characteristics of growth in different parts of the body. Likewise, it is not possible in a brief period of time to cover the treatment of all forms of cancer in all localities. Most of the discussion of this phase of the treatment of the disease



is centered around cancer of the skin the lower lip, the mouth the breast, and the uterine cervix. It may be mentioned in passing that cancers in certain locations, as the larynx and esophagus, have been more or less removed from the realms of radiotherapy, at least for the time being.

The most important point to be borne in mind in connection with cancer and its treatment is the fact that it remains a local condition for a variable time depending upon its location and degree of malignancy but always has a tendency to spread beyond access and to become a general disease. Our ability to cure it depends upon the possibility of complete eradication before it has spread beyond access to whatever agents we may have available for its complete removal or destruction. After it has become general there is no known means of curing the condition and any treatment we may direct against it is no more than a palliative measure. Other essential points in the proper understanding of this treacherous disease are a knowledge of the rapidity of metastases from cancers in various localities, the degrees of malignancy in growth and metastasis of certain types manifest by peculiar cell characteristics and the differences in reactions to destructive agencies exhibited by these different types. The first essential steps in treatment are the determination of a correct diagnosis of the lesion, its extent, and, whenever possible its cellular characteristics.

### SUPERFICIAL EPITHELIOMATA

The factors to be considered in the selection of methods of treatment of superficial epitheliomata are (1) The cosmetic effect and the desirability of a minimum loss of tissue, although the safety of the patient always takes precedent, (2) the depth of the lesion and (3) the rapidity with which metastasis usually takes place, as from lower lip cancers.

**The Eyelids**—These lesions are usually basal cell in type grow slowly and do not metastasize. The procedure of choice is the use of radium, because of the minimum loss of tissue entailed. The eyeball must be carefully protected. Electrodesiccation may be employed as an adjunct if the growth is large. Cancers

occurring at either canthus are prone to extend deeply before becoming very extensive externally. If either bone or conjunctiva is involved, the eyeball may have to be removed to provide access to the deepest portions of the growth. Many a patient has lost his life because of a hesitancy in removal of an eye under such circumstances.

**The Face**—Most epitheliomata around the face respond well to radium, and with a minimal loss of tissue. If the lesion is deep, electrodesiccation may be required in addition. These lesions usually do not metastasize. Radium is preferable to a ray irradiation in their treatment. The superficial reaction can be carried much further and with safety when radium is employed. Lesions over the temple have a decided tendency to extend deeply and sometimes heal over the surface and continue to grow subcutaneously. Occasionally they will penetrate the temporal fascia and extend for a considerable distance before the skin ulcerates again. Swelling and induration must be carefully watched for after healing of epitheliomata in this region.

**The Ear**—Only the most superficial lesions on the ear should be treated by radium alone. If the growth extends to the cartilage, a section of the ear quite wide of the growth should be removed by surgery or electrodesiccation. In regions where cartilage is covered by a thin layer of soft tissue, as in the ear, larynx, and nose, the cartilage offers a barrier for a considerable time against the spread of the growth in depth but infiltration readily occurs in the deeper portions of soft tissue next to the cartilage and the growth is likely to be far more extensive than external appearances indicate. An irradiation reaction of sufficient severity to destroy all the growth is likely to produce a severe perichondritis which is very painful and persistent and will usually require removal of the involved area of the ear eventually. It is much better to do this in the beginning. The mistake most frequently made is not to remove a sufficient amount of the ear. Epitheliomata of the external ear frequently metastasize, especially if near the anterior portion or the external auditory meatus. Epitheliomata occurring at the junc

tion of the ala of the nose and the cheek are apt to infiltrate deeply under the cartilage and to become quite extensive. Electrodesiccation is often required to supplement radium applications in this region.

### THE LOWER LIP

Success in treating cancer is proportionate to the degree of malignancy and the tendency to more or less general metastasis. The lower lip is an important area because the cancerous lesions found there are of a rather malignant type as a rule and metastasize readily and comparatively early although the metastasis is rarely as general as is the case with breast cancer and the involved secondary areas usually remain accessible for a long time. There is considerable controversy between surgeons and radiologists concerning the best methods of dealing with lower lip cancer and this is probably because each method is about equally efficacious in experienced hands. The fact that the majority of lower lip cancers are now treated by non surgical measures in many of the large clinics would seem to be ample proof of the efficacy of irradiation treatment. Success is not derived from the use of this method alone however but by the judicious combination of irradiation electrodesiccation and surgery.

We have treated our lip cases for a number of years by the following method. The primary lesion and the area for some distance beyond receives a thorough surface radium application. If the growth is very superficial this treatment of the primary lesion may suffice. If the growth is deep however and if there is a distinct induration the area is removed as soon as possible by electrodesiccation. This is carried out in such a manner

that a specimen is obtained for biopsy. We

do this because we feel that a spec-

imen is necessary over and around the primary lesion may be obtained by opening up the lymphatic channels. For the same reason we are opposed to the implantation of bare tubes or needles in or around the primary lip lesion. An ulcer resulting from electrodesiccation gives very little discomfort and a severe radium reac-

tion is very uncomfortable. Cancerous tissue gives a different reaction from that manifest by normal tissue when electrodesiccation is being employed. This difference in reaction has frequently aided us in detecting cancerous involvement beyond the area suspected. For this reason electrodesiccation has an advantage over other methods of removal of cancer bearing tissue. At the time of irradiation of the primary lesion the lymphatic channels draining the lip and the lymph gland areas in both sides of the neck are exposed to x rays and well filtered radium irradiation. We believe that unless a case is thoroughly treated in this manner it should not be treated at all by non surgical measures. The neck and face are irradiated subsequently once or twice at appropriate intervals whether glands are present or not. If glands are palpable at first or appear later and do not disappear under treatment we advocate block dissection if this is possible. Our experience with radium needles or bare tube implantations in metastatic glands has not been a happy one. Our results with postoperative treatment have not been very successful and we prefer to treat the cases throughout.

It has been a great satisfaction to us to have our cases grouped on a pathologic basis according to the method of Broders<sup>1, 5</sup> and based mainly upon the extent of differentiation of cells and the prevalence of mitotic figures. It is true that such a grouping is of value largely from the standpoint of prognosis but the pathologic classification of the primary lesion may influence the subsequent treatment of the metastatic areas to some extent. We are inclined however to treat every lip cancer as energetically as though it fell in the more unfavorable Groups 3 or 4 no matter what its prognostic classification may be.

### CANCER OF THE MOUTH

Mouth cancers may be grouped for convenience of discussion as follows: (1) Those involving the mucous membranes of the cheek, alveolar processes, anterior pillars and palate; (2) the tongue; (3) the floor of the mouth; (4) the tonsil; and (5) the pharynx. Metastasis occurs readily from all of these regions and the same care must be observed in dealing with the met

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We have treated our lip cases for a number of years by the following method. The primary lesion and the area for some distance beyond receives a thorough surface radium application. If the growth is very superficial this treatment of the primary lesion may suffice. If the growth is deep however, and if there is a distinct induration the area is removed as soon as possible by electrodesiccation. This is carried out in such a manner that a suitable specimen may be obtained for biopsy. We prefer to desiccate the growth before the radium reaction appears because we feel that a severe reaction such as we believe necessary over and around the primary lesion, may favor metastasis by opening up the lymphatic channels. For the same reason we are opposed to the implantation of bare tubes or needles in or around the primary lip lesion. An ulcer resulting from electrodesiccation gives very little discomfort and a severe radium reac-



of an application of the same severity. Surgery on the other hand was bringing about some very successful and apparently permanent results through the procedures of laryngofissure or laryngectomy. If we stop to consider the insidious and resisting nature of squamous cell carcinoma and the histologic and anatomic characteristics of the larynx the reasons for unsuccessful results are obvious. Attention has been called to the similarity of structures of the ala of the nose, the external ear and the larynx where the cartilage is covered by a thin layer of soft tissue in which the growth starts. The cartilage resists invasion for some time and infiltration readily traverses its soft tissue covering. If we consider the great care required in the treatment of an epithelioma at the attachment of the ala of the nose and cheek and transfer this growth to the larynx where it must be treated by a radium applicator placed by indirect vision *with probably only a part of the growth in sight in more or less constant motion and not always in correct position* we can readily understand the difficulty of administering a caustic dose to the entire lesion without damaging the cartilage. Severe irradiation of the cartilage is not only very painful but may destroy the best barrier against spread of the carcinoma. Well treated early lesions did seem to respond most successfully in many instances but there was invariably a fatal recurrence. The only treatment we now employ in laryngeal cancer is palliative deep x-ray therapy in inoperable cases and post operative applications also by high voltage x-rays using the *fractional daily dose or the saturation method*. After laryngectomy the latter procedure cannot injure cartilage and is directed against a growth that is really metastatic if present.

### THE ESOPHAGUS

Before giving up the treatment of esophageal cancer by direct radium applications we had reached the conclusion that such applications were futile unless the exact extent and location of the growth was determined by esophagoscopy. Even then we realized that the problem of keeping the applicator in proper apposition to growth was still more difficult than in the

treatment of laryngeal cancers. The rather extensive experience of the late Dr. R. Walter Mills and Dr. Kimbrough<sup>7, 8</sup> and presented in detailed reports before the American Radium Society in 1922 and 1925, seemed to prove that radiation, even when carried out by the very best technic, could not be regarded as more than a palliative measure. Life was apparently prolonged in some cases, mainly by the temporary increase in the lumen of the strictured and ulcerated area of the esophagus. It occasionally happens, as noted in the earlier report of Mills and Kimbrough, and as observed in our own experience, that a carcinomatous lesion may be apparently healed by local radium treatment; but later on another growth will be discovered lower down, either at autopsy or by esophagoscopy. This is due, of course, to the deep distribution of the lymphatics along the continuity of the esophagus.

It is a fact that cancer of the esophagus is not diagnosed as early as it should be. The usual routine examination by liquid suspensions of bismuth or barium will not detect any but the late lesions. The swallowing of the capsule should be a part of the routine gastro-intestinal study, and should always be employed in obscure cases of substernal pain or slight dysphagia. Lodgment of the capsule calls for an esophagoscopy if it cannot be satisfactorily explained. We doubt, however, that results will be any better when diagnoses are made earlier in the progress of the disease.

For the past year or two we have felt that direct radium treatment for cancer of the esophagus is hardly worth while, and have discontinued it.

#### UTERINE CANCER

The relative merits of irradiation treatment for cancer of the cervix has been rather definitely settled by the report of the investigations of the Cancer Commission appointed by the American College of Surgeons several years ago.<sup>10</sup> Statistics have been unusually reliable in these investigations and the report of the Commission has been rather generally accepted as a fairly accurate estimate of the relative merits of radium and surgery, the former having a little the better of the argument.



Radium results may be modified somewhat by the use of deep x ray therapy as a supplementary measure. It narrows down to which method is able to reach the furthest outlying cancer cells. Radium is limited in its effect but may kill cells a little further out than they can be reached by surgery or it may have the advantage of encapsulating cells that could not be reached at all by operation and keeping them dormant for a time. Operation seems to be the procedure of choice in early cancer of the fundus.

### CANCER OF THE BREAST

This is the most important seat of cancer around which to center a discussion at the present time upon the relative merits of irradiation. Before drawing any definite conclusions it is important to discuss certain phases of the subject more or less in detail.

1 Numerous attempts have been made in recent years by various authors to compile statistics that would indicate the exact status of irradiation but in most instances they have failed to present the situation in an exactly correct manner. In a recent article by Daland<sup>12</sup> the average duration of life in 100 untreated cases of carcinoma of the breast was compared with that of 66 cases treated by various procedures. In the 100 untreated cases the average duration of life was 40.5 months. The only direct comparisons that could be made between the untreated and treated cases were the facts that in the former group 40 per cent were living at the end of three years and 22 per cent at the end of five years whereas in the treated group the figures for corresponding periods were 60 and 42 per cent respectively. In reality these figures tell us little or nothing of what we really want to know. The reasons are obvious after a little reflection and need not be commented upon. In 1925 Lee and Herendeen<sup>13</sup> published a report of 92 cases of breast cancer treated between 1919 and 1922. For our purposes their statistics may be summarized as follows:

	Cases
Preoperative and in most instances postoperative irradiation	31
Postoperative irradiation only	36
Surgery alone	25

Alive and well in 1925	Per cent
Preoperative cases	52
Postoperative cases	59
Surgery alone	24

The authors enter into the subject much more in detail of course. The trouble with their statistics is that they have endeavored to prove too much by too small a number of cases and that their work is that of a single group of men. Nevertheless they are working in the right direction.

Many other excellent statistics could be quoted but they are generally along similar lines, are more or less individual and have very little actual value. Our own impression of statistics on breast cancer is that anyone can prove almost anything he wishes by them. We are not particularly interested in what one man can do. A few years ago I read a paper in which it was shown statistically, among other things, that a group of untreated cases lived many years longer than other selected groups treated by surgery alone, preoperative and postoperative irradiation. This paper was not published because of the likelihood of its having been misunderstood.

The statistics which are really needed are those compiled from the best men of the country covering a large number of cases treated by surgery alone, by preoperative or postoperative irradiation, and by both combined. One group of statistics should cover strictly operable cases and there should be further modifications of groups to include cases with axillary gland involvement and possibly other features. Moreover each pathological or prognostic group of breast cancers should have its own statistical tables. Surely this is a prodigious undertaking but until it is accomplished the less the controversy over the unknown the better.

2. Probably the most important investigations that have yet been carried out in connection with breast cancer are along the lines of attempting to group the various lesions according to degrees of malignancy in a manner similar to the work of Broders<sup>1-2</sup> in his lip and mouth cancers. Greenough<sup>3</sup> has presented this subject to us in a very simple manner which may be summarized as follows:

<i>High Malignancy</i>	<i>Low Malignancy</i>
1 Little differentiation—cells arranged in solid columns	1 Good differentiation—adenomatous arrangement of cells
2 Variations in size of cells and nuclei—large and small mixed together	2 Uniformity in size of cells and nuclei
3 Cells without secretory function	3 Cells showing secretory function
4 Hyperchromatism in nuclei in high degree	4 Absence of or slight hyperchromatism
5 Numerous and irregular mitoses	5 Few mitoses

This table represents Groups 3 and 1 respectively and there is also a middle group. It is obvious that the best results by any method of treatment will be obtained in Group 1 cases and that those of Group 3 are practically hopeless by any method of treatment unless it can be regarded as palliative only. Unfortunately this grouping must be made after operation and it cannot be applied to preoperative irradiation. It may serve as a selective procedure in justifying postoperative treatment.

3 The metastases from cancer of the breast are most interesting and unusual and are probably too little considered in the controversy over methods of treatment and in formulating opinions as to the exact merits of surgery and radiation. The exact time of their occurrence is very uncertain and variable but no doubt has some connection with the pathologic type of the primary lesions. It is a progressive disease and tends in time to spread throughout the body but again the time of its spread beyond the nearby lymph nodes is variable. Personally I have in the past year become a firm believer in the permeation theory of metastasis from breast cancer as expounded by Handley<sup>1</sup> several years ago but recently modified by Carnett<sup>16</sup> after his studies based upon Roentgen ray examinations, autopsies and clinical investigations. When we consider the nature of such metastases there is nothing we can do when they have already taken place to save the patients and the best we can hope for is a prevention of local recurrence by irradiation and a modification of important secondary foci as in the bones until the patients finally succumb. We probably see more wide spread metastases now than a few years ago because we keep many patients alive longer.

4 Surgery is now and will continue to remain the only safe and sane method of dealing with early and still localized cancer of the breast. The question as to whether operation is permissible when the disease has crossed over the borderline of absolute operability we believe to be still an open one especially in individual cases. There is often an excuse for it if we are to regard postoperative irradiation of any value but no one should feel free to operate routinely on the so called inoperable cases simply because he has postoperative treatment to fall back upon. We have certainly seen the advantage in removing a breast alone by a so called palliative operation when at first, it was more or less fixed and inoperable, but later rendered movable and operable by irradiation.

In spreading the teaching of early operation we firmly believe that the so called benign tumors of the breast should be regarded as potentially malignant if let alone. No argument yet offered has been sufficient to convince us otherwise. We have seen many cases of cancer which gave a history of a lump of many years' standing before the apparent advent of carcinoma but no case coming to us with a tumor present for a long time has turned out to have a benign lesion. The clinical diagnosis of benign tumor is by no means infallible and secondary operations are not uncommonly required following biopsy, and in the hands of the best of men. We believe, also, that cystic mastitis may be a forerunner of cancer, though of course, not always. We have seen enough cases with a history of mastitis in both breasts and with carcinoma developing in one and later in the other, to convince us that there is a distinct element of danger in the condition. As the condition may develop into cancer, all cases should be carefully watched. When patients are referred to us with this condition, our present plan is to use the breast pump as recently proposed by the Staff of the Memorial Hospital and to supplement this procedure by x ray treatment.

5 Irradiation is certainly indicated in breast cancer under many circumstances. After the condition has become more or less general, whether this fact is known or not, irradiation therapy in the presence of inaccessible metastases can be regarded simply

as a highly developed scientific makeshift for a better and hoped for cure of the future but at the present time it is the best we have and its use is certainly desirable whenever any benefit is possible

It is not our purpose to minimize in any way the use or good effects of irradiation therapy. Before anyone propounds its virtues or criticises its uses its exact effects or its possibilities or emphasizes its shortcomings its action should be thoroughly understood. The effects of irradiation upon cancer bearing tissue are numerous. The ideal one is of course the direct destruction of carcinoma cells. While this is the usual and possibly the only means of complete cure there are other reactions which may be of benefit in a more or less palliative way. Lymphocytic infiltration is probably a result of cell degeneration and subsequent fibrous tissue formation is a means of encapsulation of remaining viable carcinoma cells which may lie dormant for a variable time. The obliteration of blood vessels causing partial devitalization of the growth and of lymphatic channels preventing spread of the cells are effects about which pathologists differ. The production of immunity is a term we are fearful of using although many of us who see a large number of cancer cases have a subconscious feeling that there may be something of the kind. Like an individual resistance that might bear a modified name to satisfy the censors. Possibly Broders term of cancer's self control<sup>4</sup> might not be so open to criticism. The old controversy over stimulation is always apt to come up for discussion when considering irradiation effects. Many of us who are growing old in experience with x ray and radium therapy feel that it is very difficult to give up the thought of stimulation. We usually compromise by agreeing to limit our beliefs to the fact that a cancer irradiated by too small a dose may in time recover and its recovery may be attended by a more vigorous growth. There is no doubt that an overirradiated tissue may sometimes become a more favorable soil for subsequent cancerous growth.

**Indications**—Irradiation may be regarded as indicated for purposes of discussion under the following conditions

1 *Preoperative Treatment*—At one time we were very much impressed by the theoretical possibilities of irradiation before operation, but we had a rather unhappy experience in the group of cases in which it was carried out. Most of them recurred rather rapidly, even with postoperative treatment. Possibly they belonged to the unfavorable pathologic group. We have not determined this. But at any rate, we abandoned the procedure, and have been waiting for some dependable statistics to show us its exact value. There is some difference of opinion as to the more favorable time for operation when preoperative irradiation has been carried out. Immediate operation has its advantages, but the influence is then exerted only upon the cancer cells within range of a lethal dose. Some will argue that the fewer the viable cells remaining, the less the chance of metastasis occurring as a result of the operative procedure and an early effect is exerted upon any cells that may be left. Irradiation has a depressing effect upon some patients and it is a question as to whether this is desirable just at the time of an operation. There is probably little deleterious effect upon the normal tissues as regards healing unless the skin flaps are very thin. If operation is deferred for a month or six weeks the full effect of the irradiation is exerted, and if there is any such thing as the closing off of lymphatics it is given the opportunity to take place. Moreover, the growth may diminish in size and has been known to disappear. On the other hand, the time of waiting for the ultimate effects gives an additional period for metastasis to occur. We are not so sure that *severe* reactions may occasionally favor metastases, as has previously been mentioned in connection with the lip. Needles should not be used. Most of our cases were given rather severe reactions. We are uncertain, therefore, about the whole procedure, and, as previously stated, we are waiting, and are open to conviction.

2 *Postoperative Treatment*—The crux of the whole situation really rests upon this aspect of treatment. Shall we give it or not? The question can never be answered correctly until the proper statistics are forthcoming. Correct statistics bearing on this situation will be very difficult of compilation, especially as

as a highly developed scientific makeshift for a better and hoped for cure of the future but at the present time it is the best we have and its use is certainly desirable whenever any benefit is possible

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## American College of Surgeons

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If recurrence should become apparent during the rest period earlier treatment would have done no good anyway in such a malignant case. Waiting for recurrences to become evident before beginning postoperative therapy may favor metastasis and is not a wise compromise to replace routine postoperative treatment.

3 *Palliative Treatment*—In properly selected inoperable and recurrent cases there is no question that considerable comfort may be obtained by irradiation. There is no necessity for prolonged discussion of this subject.

4 *Primary Operable Cases Inoperable Because of Age or Intercurrent Disease*—In such cases it is fortunate that we have some means of more or less controlling the outward evidences of the disease. It has frequently been argued that favorable results obtained in such cases warrant the use of irradiation alone in any operable case. This has not been our experience. One patient came to us for treatment of a small lump in the breast six months after its discovery. She had refused operation. The growth disappeared after six months of treatment. Over a year later we found multiple bone metastases. Operation at the proper time might have prevented the spread of the disease. In another instance operation was regarded as inadvisable because of age in a woman with a moderate sized carcinoma of the breast and a low lying axillary gland. x-Ray treatment produced a temporary increase in size but there was a subsequent subsidence to less than the original dimensions. Radium needle implantation was followed by rapid enlargement, ulceration and extensive metastasis. We believe this was an instance in which the patient would have been better off without any treatment. Such cases as the last one are exceptions and should not be used as arguments against measures which do good to a large number of other individuals.

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## CLINIC OF DR. JOHN BERTON CARNETT

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### THE DIAGNOSIS OF EARLY CANCER OF THE BREAST

THE most serious obstacle to the cure of cancer by present-day methods is the disastrous delay between the onset of cancer symptoms and the institution of cancer treatment. Cancers in many regions, including the breast, yield a high percentage of permanent cures by treatment during the earliest stage. Treatment which is first undertaken during the late stages prolongs life and comfort, but seldom cures. The death rate from cancer can be materially diminished only by earlier diagnosis.

Over 100,000 people die of cancer every year in the continental United States. Cancer of the breast is responsible for 10,000 of these deaths, a big percentage of which might be averted by timely treatment. An analysis of the deaths from all causes occurring over the age of twenty years here in Philadelphia shows that in 1923 1 out of every 10 and in 1924 1 out of every 9 were due to cancer in some form. Cancer is so appallingly prevalent that we clinicians should keep its possibility in mind in every case in which a diagnosis is at all obscure.

Past delays in treatment have been due in part to ignorance, indifference, or fear on the part of the patient in making a first visit to any physician and in part to failure of the physician first consulted to make a prompt diagnosis and compel the patient to undergo treatment at once.

The laity are being taught through various channels and we also should endeavor to instruct our patients and friends that the signs which are suggestive but are not pathognomonic of cancer of the breast are (1) any lump in or near the breast or in the armpit, (2) any discharge, whether bloody or not, from the nipple,

(3) any acquired distortion or inversion of the nipple (4) any appreciable enlargement or diminution in the size of one breast (5) any puckering of the skin over one breast or (6) any abrasion or ulceration near the nipple

Upon the discovery of any one of these signs the patient is urged to report to a physician within the first twenty four hours. It then becomes our duty to arrive at a diagnosis including a consultation if necessary within the next forty eight hours and if cancer is present or cannot be eliminated the patient should be sent to the hospital within the next forty eight hours for treatment or for operative exploratory diagnosis. Each day's delay beyond the preceding program in establishing diagnosis and instituting treatment for cancer of the breast is just as reprehensible as each hour's unnecessary delay in arriving at a diagnosis and applying treatment in a case of diphtheria gangrenous appendicitis or strangulated hernia. Delay in cancer diagnosis and treatment tends to a fatal outcome just as inevitably as in the specified more acute affections even though the cancer death be more remote and incidentally attended by greater distress and suffering.

The active campaigns carried on to instruct the public in the earliest symptoms of cancer and in the importance of early treatment are resulting in many patients seeking professional advice at a very early stage of the disease. It is therefore imperative for us clinicians to familiarize ourselves with the earliest symptoms and signs of the disease. In studying cancer literature we should focus our attention on the opening paragraphs dealing with symptoms and diagnosis of cancer in the earliest stage. In the past our attention has too frequently been directed to the closing paragraphs dealing with the late or undertaker's stage of the disease.

The family history and the previous personal history except as they pertain to the duration and progression of breast symptoms are of no importance in arriving at a correct diagnosis in any individual case of breast cancer. Under ideal conditions the only history we ought ever to obtain is that the patient first noted some breast abnormality within the past twenty four hours and

the note act ought to be read to any patient giving a breast history of longer duration

In approaching a breast lesion the most important points we have to bear in mind are that (1) cancer is the most common of all causes for definite lumps in the breast of non lactating women over twenty five years of age (2) any such lump should be regarded as cancer until proved otherwise and (3) if cancer cannot be positively excluded within the first forty-eight hours the patient must go to the hospital within the next forty-eight hours to have a definite diagnosis established

The Pennsylvania Cancer Commission found that in 1910 the physicians first consulted for cancer of the breast did not make a local examination in 3 per cent of the cases For the sake of the medical profession of Pennsylvania I am glad to state that this disgraceful carelessness was not encountered in a single instance of breast cancer in 1923 A proper examination of a breast cannot be made except by having the patient remove all clothing above the waist line

The usual cause which brings the patient to the clinician is the accidental discovery of a lump in the breast By the time a lump has attained sufficient size for it to be discovered by the patient's unskilled palpation it has usually developed enough characteristic changes for the trained fingers of the experienced clinician to arrive at a correct diagnosis Males females under thirty five years of age and lactating women are not immune but they furnish only a small percentage of the total number of breast cancers

Palpation is the most valuable single method of examination for early cancer but it should be conducted with the utmost gentleness Vigorous palpation dislodges cancer-cells which may be carried as emboli to cause distant metastases Every area in both breast both axilla and both supraclavicular regions should be systematically examined in every case of suspected breast lesion The breast should be palpated both by picking up successive areas between the thumb and fingers and by gently compressing and sliding the breast tissue back and forth against the chest wall by means of flat fingers

The earliest clinical evidence of cancer of the breast is obtained by palpation and consists in the finding of a definite irregular hard non sensitive lump that cannot be moved independently of the breast and that shades away gradually into the adjacent breast tissue without any clearly defined line of demarcation between tumor and breast tissue in a non lactating woman over thirty five years of age. The discovery of such a lump without any further evidence demands immediate hospitalization of the patient for radical amputation or for operative diagnostic exploration. The worst possible course of procedure for us to pursue in a breast tumor of that type is to have the patient return to our office week after week in the futile expectation that we will find more conclusive evidence at each succeeding visit or that applications of antiphlogistic ichthyol mercurial ointments or any other drugs or nostrums will avail in causing the tumor to disappear. Massage and rubbing never benefit any breast lump and they do irreparable harm in cancer. Our text books teach that cancer grows rapidly but its speed is only relative in comparison to the far slower growth of benign tumors. Except for some rare varieties cancer is always a very slow growing tumor and it is only after a lapse of many weeks or months that we should expect to detect sufficient progression of the disease to aid materially in the diagnosis.

The slight increase in size of the primary growth is of minor consequence as compared to the very grave danger of distant inoperable metastases taking place as the result of a waiting policy. None of us can determine at what hour or moment a sneaky insidious metastasis may extend far afield and convert a favorable local lesion into a hopelessly incurable one.

We should regard cancer as a semi emergency lesion and force the patient into the hospital at the earliest possible moment to forestall the distant metastases. After admission to hospital the surgeon will not proceed to instant operation as he would for strangulated hernia but will spend twenty four to forty eight hours in thorough study both of the local lesion and of the patient's general condition before arriving at a decision as to operative or non operative treatment. If the diagnosis of cancer is

uncertain an exploratory incision with fairly wide removal of the growth for gross inspection or frozen section microscopic examination or both is indicated before resorting to an amputation which if necessary must be done during the same anesthesia and not a week or more later. Ordinarily radical breast amputation without preliminary exploratory incision followed by postoperative radiation is the preferred treatment in the cases in which the diagnosis of cancer is certain.

Unfortunately cancer of the breast does not cause pain or tenderness until the late stages. The pernicious and fallacious dictum "If your lump does not bother you then don't bother it" is prevalent with the laity and some physicians and has all too frequently been responsible for delayed treatment and for needless suffering and deaths. Absence of pain and tenderness in a breast lump must never be construed as evidence against early cancer. On the other hand a mild trauma as from the proverbial broom handle striking a previously unrecognized breast cancer may cause pain and tenderness out of all proportion to the mildness of the blow. We clinicians should be on the alert to suspect cancer when we find undue pain, tenderness and swelling or lump following slight breast injury.

Many patients whose only complaint is pain in one or both breasts seek examination because they fear it is caused by cancer. The most common cause of breast pain in the absence of a lump is neuralgia of one or more of the third to the sixth intercostal nerves and its presence can be demonstrated by finding tenderness along the trunks of the affected nerves in the intercostal spaces at the outer side of the breast, in the upper axilla, at the posterior margin of the scapula when the latter is pulled forward by the patient folding her arms and also under the breast when the latter is not too firmly attached to the chest wall to permit palpating fingers to be inserted behind it. Intercostal neuralgia may be coexistent with but independent of cancer or any other lesion of the breast. The pains in the breast which the text books commonly ascribe to chronic cystic mastitis are usually due to intercostal neuralgia. Pain is the usual cause of breast cancerphobia. Simple denial of the presence of cancer fails to

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years, but thereafter they should all be removed by simple excision of the tumor except in the case of chronic cystic mastitis, which should be treated by excision of the entire breast.

It is only rarely in the past that the surgeon has encountered a breast cancer at the early stage described in the opening paragraphs of this paper. We hope to discover them more frequently in the future in patients who apply either for routine health examinations or for prompt diagnosis of their recently discovered breast tumors. When the patient is first seen at a slightly later stage it is usually possible to demonstrate the important diagnostic symptom of cutaneous dimpling over the cancer by gently tensing the skin over it. This confirmatory sign of cancer is elicited by gently lifting the whole breast forward while observing the tumor region for evidence of flattening or dimpling of the skin. In this same early stage there may be a slight thinning or absorption of overlying fat which is suggestive of cancer. It is only in the late stages that skin dimpling (orange-skin or pig-skin appearance) is so obvious that it need not be sought for by tensing the skin.

In some cases retraction, fixation, or distortion of the nipple occurs early, in others none of them may develop even in the late stages. A depressed nipple is not necessarily due to cancer. The earliest evidence of nipple involvement is best detected by comparing the response obtained in attempting to draw each nipple away from its breast and finding firmer fixation and less range of motion on the affected side. Distortion of the nipple is most obvious in the sitting or standing position. The ducts first involved by the cancer are the first to be drawn inward, with the result that the nipple tends to tilt toward the site of the cancer.

Enlarged axillary lymph-nodes may be present in benign breast lesions and often may not be demonstrable before operation in many late cases of cancer, hence the presence or absence of enlarged nodes is not a vital sign in the differentiation of a benign from a malignant lesion. Exceptionally the first sign of cancer to attract the patient's attention may be enlarged lymph-nodes in the axilla or along the under edge of the pectoralis major muscle. Any patient having these enlarged nodes in the



absence of an obvious focus of pyogenic infection should be suspected of having breast cancer and diligent search should be made to detect its possible presence

Some patients seek advice solely because of discharge from the nipple. Bloody discharge occurs in only a small percentage of the total number of breast cancers and it is usually due to a primary papillary epithelioma of a duct or to benign intracystic papilloma. The latter lesion has a tendency to become malignant hence both of them should be subjected to early operation. Unfortunately bloody discharge may very rarely be encountered in other benign lesions which do not require operation but in cases of doubt exploratory incision is indicated. The segment of the nipple occupied by the discharging duct orifice corresponds to the segment of the breast into which the duct radiates and therefore indicates the breast segment which needs particularly to be examined or incised.

In exceptional instances an eczematous involvement of the nipple or areola may be the only symptom which leads the patient to the diagnostician. True Paget's disease of the nipple and areola which is an eczematoid lesion of many months or years duration before it undergoes cancerous change is a very rare affection and the onset of malignancy is suggested by a slight infiltration or brawniness of the skin. More commonly pre existing cancer of the breast situated in or near the nipple is the primary lesion and the skin erosion is secondary to it. The presence of cancer is indicated by finding an indurated lump in or behind the nipple or areola or by parchment like infiltration of the skin. Simple eczema may occur in this region but it does not infiltrate the skin. In case cancer cannot be excluded an immediate biopsy is indicated.

An occasional patient seeks advice because of an alteration in size or contour of the breast. A breast may be contracted by scirrhous cancer or enlarged by the softer forms of cancer and may be distorted by either variety. Careful palpation will disclose the tumor as cancer reaches a late stage before it distorts the breast. Inequality in the size of the two breasts is not rare in the absence of cancer.

Fixation of the breast to the pectoral fascia or chest wall, cancerous invasion of the skin with impending or present ulceration, easily palpable axillary or supraclavicular lymph nodes distant metastases to the liver, lungs or bones general anemia loss of weight, and cachexia are all very late symptoms which should be forestalled by earlier operation.

Late cancers of the breast are nearly all incurable. The earlier the diagnosis and the earlier the treatment, the greater will be the number of cures. The earlier the lesion and therefore the more uncertain the diagnosis the brighter is the prospect of cure. We should be constantly on the alert to detect cancer in the early stage and to avoid any form of procrastination in arriving at a definite diagnosis in every suspicious case. Furthermore, it is our obligation in every case in which we advise operation or exploratory diagnosis (1) to make immediate arrangements for the patient to enter the hospital and (2) to follow her up till we know she has entered the hospital, otherwise she will wander from pillar to post seeking a more favorable opinion and thereby lose her golden opportunity for early treatment. Until some entirely new form of treatment for cancer is discovered our percentage of successful results is directly dependent upon the earliness of diagnosis and treatment.



## CLINIC OF DRS P O SNOKE AND W P BELK

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### MULTIPLE PRIMARY TUMORS OF THE SKIN

MULTIPLE primary epithelial tumors of the skin, probably because of their comparative rarity and marked differences in appearance have been variously classified and named. This has made it difficult to identify cases under study with similar cases in the literature, and has probably led to the belief that tumors essentially similar constitute distinct pathologic entities.

MacLeod<sup>1</sup> advances a theory that seems to harmonize the various opinions on this subject and offers a satisfactory basis for the understanding of these varied growths. He says 'It seems probable that they are derived from groups of embryonic cells (cell rests of Cohnheim) which if they fulfilled their developmental intention would have developed into either epidermis, a pilosebaceous follicle or a sweat gland and that they belong to the class of nevi and may be designated 'nevi-cyst epithelioma tosa'. He gives a list of the various terms used to designate such lesions which is copied here that it may aid others in searching records for reports: Adenoma of the sweat glands (Perry), Svingocystadenoma (Torok Unna), Epithelioma kystique benign (Jacquet), Cylindroma of the skin (Nicolau), Trichoepithelioma papulosum multiplex (Jarisch), Nævi epitheliaux kystique (Besnier), Hæmangendothelioma cutis papulosum (Jarisch), Epithelioma adenoides cysticum (Brooks).

The marked dissimilarity in appearance between the two examples of multiple skin tumors here reported, their rather similar clinical course and their identical histogenesis as interpreted by us illustrate well the application of this theory.

## CASE I

E. W., a white spinster aged sixty-seven, came to the Philadelphia General Hospital January 19, 1926 complaining of a "growth on her head."

In 1922 she noticed a small "wen" over the vertex, which ruptured four months after discovery, bleeding slightly, but causing no pain or discomfort. It remained about the size of a walnut for two years. In 1924 the mass "came off," but one week later it began to grow again. The past medical and social



Fig. 245.—Case I. April 30, 1926.

history are unimportant. She states that her mother had a similar growth on her head.

Examination upon admission revealed a cauliflower-like, bleeding mass, the size of an orange, in the midline over the vertex. It was fairly movable on its pedicle, but not indurated. In the frontal region two nodules were felt in the skin the size of marbles. Posteriorly there were also two nodules (Fig. 245). These were intradermal, very hard, and not as well circumscribed as the usual sebaceous cyst. The lymph-glands in the neck were slightly enlarged.

x Ray plates of the skull showed no evidence of bony involvement

On February 25, 1926 an erythema a-ray dose was given over this tumor and a radial excision was performed March 3, 1926 (Fig 247), removing the mass down to the periosteum over an area 5 cm in diameter This area healed slowly and a skin-graft was done March 22, 1926, but with only moderate success (Fig 245) Patient was discharged from the hospital May 30, 1926, with complete healing of the operative site, and reported



Fig 246 —Case I December 27, 1926

to the Follow up Clinic regularly, showing no recurrence (Fig 246) When she reported in December, 1926 it was thought of considerable importance to know what the other nodules were Two of these were removed on January 12, 1927 and proved not to be sebaceous cysts The walls were not well defined and only one of them contained fluid The two incisions healed by first intention, with no recurrence since

The present condition of patient is excellent No evidence of recurrent growth in any of these lesions has been seen A series



Fig 247—Case I The tumor removed March 3 1926



Fig 248—Case I Photomicrograph showing general character of tumor  
( $\times 35$ )

of radium pack treatments were given over the area from which the original growth was excised

The specimen (Fig. 247) consists of a piece of scalp to which is attached by a broad base a pedunculated tumor 6 x 6.5 x 2 cm. The growth is deeply lobulated and superficially eroded. The cut section is whitish and divided into small circular areas by fibrinous bands (Museum 7014—011,7912).



Fig 249.—Case I Photomicrograph showing edge of one of the globular masses shown in Fig 248 ( $\times 230$ )

The essential microscopic characteristics of several biopsies of the tumor were so nearly the same that one description will serve.

Extending rather deeply into the dermis are multiple oval masses of hyaline and grumous material, surrounded by and evidently derived from a layer of squamous cells (Figs. 248, 249). These cells rest on an unbroken basement membrane, and vary from a type closely similar to that seen in the deeper layers of



the skin to that on the surface of this membrane. These surface cells are keratinized and merge with the hyaline material forming the center of the masses. These globoid structures are 1 to 4 mm in diameter, though there is considerable variation in size. Those most characteristic, that is, most representative of the average, have no rete pegs, nor can any prickles be seen. Near the true skin surface, however, a few prickles appear.



Fig. 250 —Case I. Photomicrograph showing more cellular areas ( $\times 57$ )

and here and there definite pegs. Whether these be of the skin itself or of the tumor cannot be said, as the two structures merge together. In some areas there are a greater proportion of well-preserved cells and less hyaline material (Fig. 250). Here typical pearly bodies appear, but usually without prickles. The cells in these areas are of the intermediate squamous type, and quite suggestive of hair-follicle cells. In some areas the hyaline material is calcified; in others giant-cells appear, evidently the re-

sult of the mass of inactive matter. All the masses are well encapsulated.

This lesion is aptly described as a small section of dermal tissue turned outside in. The desquamated epithelial cells normally shed from the surface of the skin, being unable to escape, collect in the cyst-like spaces, forming the hyaline balls.

The dermal anlagen in this case appears to be chiefly that of hair-follicle sheaths, the absence of rete pegs and of prickles even in the keratinized cells adding weight to this opinion. The type of cell in many places is sufficiently anaplastic to give rise to a diagnosis or a strong suspicion of malignancy, and the deeply placed pearly bodies add to this impression. Such a diagnosis would be justified on the histologic appearance alone, but gross appearance, clinical history, and knowledge of this group of tumors justify placing this among the cases of benign cystic epithelioma.

## CASE II

O. S., a well-developed Italian male aged fifty-six, was perfectly well until October, 1925, when he began to suffer with a slowly growing swelling in the skin of the left parotid region. He was employed as a belt sander by the Victor Talking Machine Co., and reported to their dispensary; from there he was referred to his family doctor because he was unable to work. In November, 1925 he was referred to Mt. Sinai Hospital for diagnosis. Upon admission there two reddish masses were present on the left cheek just above the mandible and anterior to the angle of the jaw. One of these was slightly ulcerated. They were firm, intradermal, not tender, and not attached to bone. A biopsy was performed and a diagnosis of round-cell sarcoma was made. At that time he had a leukocytosis of 14,000. x-Ray plates showed no involvement of the mandible. A few x-ray treatments of short duration were given.

The growth decreased in size, but did not disappear, and he was referred to us for x-ray therapy. The improvement was so marked that he did not report to us at once; however, January 6, 1926 he appeared, complaining of a marked subcutaneous swelling in the left parotid region. This was the size of the palm

of a hand and about as thick. The skin was not involved but an ulcer 2 cm in diameter was present. The incision for the biopsy had not healed and the ulcer resulted. In the left submaxillary and left supraclavicular regions there were several enlarged lymph nodes. These were situated deeply so that discrete nodules could not be palpated.

Treatment was started January 6, 1926 and completed January 19, 1926. Eight treatments of 20 milliamperes minutes each  $\frac{1}{2}$  mm cu filtration 14 seconds S G 50 cm S T D cross fire from right and left sides of face and neck were given.



Fig 251 —Case II May 22 1926

On January 19th the lesion was entirely healed and the tumor mass in the cheek had disappeared (Fig 251). Treatment was started February 16th over the supraclavicular mass. A short series of six treatments was given over this area of 40 milliamperes minutes each. He showed no evidence of tumor growth until March 17, 1926 when all the original tumor having disappeared, two skin nodules appeared one in front of the tragus of the left ear the other in the skin of the left cheek (Fig 252). These nodules began in the skin as reddish pimples which increased to 3 cm in diameter in about three months. The edges rose  $\frac{1}{2}$  cm sharply from the normal contour of the skin of the face,

with distinct rolling and crenation of the edge. The surface of the lesion was almost flat, pink, and showed an occasional dilated venule. They were freely movable, painless, and non-ulcerative. These appeared to be similar to those originally shown. A series of eight deep x-ray treatments were given over the nodules on the face, covering the period from May to August. There was a marked regression in these nodules, but they did not completely disappear.

Physical examination August 30, 1926 revealed a mass the size of a hen's egg in the left supraclavicular region. In the right

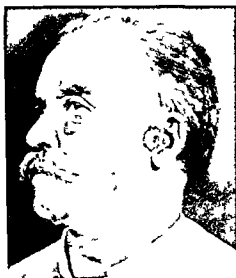


Fig. 252—Case II November 4, 1926

inguinal region a similar mass was present and also some small lymph-nodes. These smaller nodes were present on the left side also. On the anterior surface of the left thigh there was a cutaneous mass the size of a quarter and about  $\frac{3}{4}$  inch thick. Similar but smaller areas were present on the forearms. These then began to appear over the abdomen and lower right chest, varying in size, some becoming the size of a hen's egg (Fig. 253). Only one small group was found on the patient's back (Fig. 254).

A long series of daily x-ray treatments were given; 10 milli-ampere minutes being given over each group of nodules. These began July 26th and ended September 9, 1926. The factors were

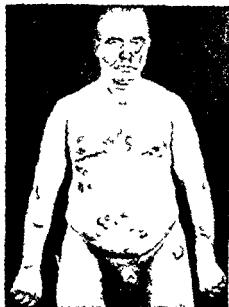


Fig 253 —Case II November 4, 1926



Fig 254 —Case II November 4 1926

two minute, 5 milliamperes 9" S. G ; 50 cm. S. T. D., and 5 mm. Al. filtration.

The general reaction to treatment was a complete disappearance or marked regression after the first treatment; subsequently a return to the original size. The character changed markedly. The red, wrinkled, raised area of the nodule became purple and smooth, and the edges, instead of rising sharply from the skin as originally seen, merged gradually with it, the consistency became jelly-like rather than fleshy.

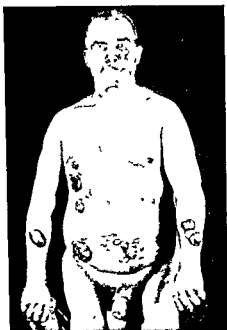


Fig. 255 —Case II. February 9, 1927.

The disease progressed rapidly, many skin nodules appearing over the entire surface of the body. They did not ulcerate until recently (Fig 255). On January 6, 1927 a large nodule was removed from the anterior abdominal wall for biopsy.

x-Ray plates of the bones and lungs were negative for metastases. Wassermann was negative in the blood.

Clinically the patient suffered no pain or discomfort. He would have been able to work except for the appearance he presented. He had never been bedfast. The temperature, pulse, and respiration rates were normal.

**Pathologic Report**—One biopsy taken at another hospital was diagnosed sarcoma of the skin. This mass was removed from the skin on the cheek at a point midway between the angle and symphysis of the lower jaw.

Through the courtesy of this hospital a copy of the section was received and restudied. Macroscopic description is not possible, as the original tissue was not available.



Fig. 256—Case 11. Photomicrograph of section from original tumor on cheek. The type of tumor cell is shown. The oval body is considered a rudimentary hair follicle.

The tumor consists of cells of no adult type, being polyhedral generally, and varying somewhat in size and staining. They are arranged in cords and in small masses where most abundant, but near the periphery of the growth, where fibrous tissue predominates, irregular arrangement is the rule and many cells are spindle shaped. The growth shows very little vascularity. It is not encapsulated, though fairly well limited by the surrounding

fibrous tissue, and in places by a reactive lymphocytosis. The growth is evidently a dermal one, but it is definitely not of the epiderm, though it touches it in places. There are present throughout the tumor a fair number of small collections of cells of a spindle variety, denser at the edges, but forming solid groups. They are surrounded by a definite narrow capsule of fibrous tissue. Though unlike any adult structure, they strongly suggest undeveloped hair-follicles (Fig. 256).



Fig. 257.—Case II. Photomicrograph showing subdermal location of tumor removed January 6, 1927.

The specimen taken January 6, 1926 is an entire tumor from the wall of the abdomen, measuring 10 x 12 mm. The overlying skin is atrophic, but it is not at all connected with the tumor (Fig. 257). The cells are fairly large, round or oval, and show some variations in size and staining. At the margins, where the fibrous tissue is abundant, the cells are spindle in shape. There is a fair amount of cytoplasm about the nuclei and the whole is a



little larger than the usual nevus cells though the lesion suggests nevus in its location and extensions. Several well formed ducts appear always running toward the skin (Fig 258). These however are lost in the mass of the cells. In the deeper parts there are many cyst like spaces lined with flat cells either endothelial cells of dilated capillaries or flattened tumor cells (Fig 259).



Fig 258—Case II Photomicrograph showing ducts in midst of tumor

The definite duct like structures identify this tumor histologically. They are not only in the tumor but of it as their cells merge indistinguishably into those of the tumor. The ducts are sufficiently like those of sweat glands to represent a development from the anlagen of this adult tissue. This tumor may then be placed with the first case under the general term benign cystic epithelioma.

The fact that this class of tumor is generally benign and re

sponsive to local surgery and radiation, makes its differentiation from more malignant lesions important

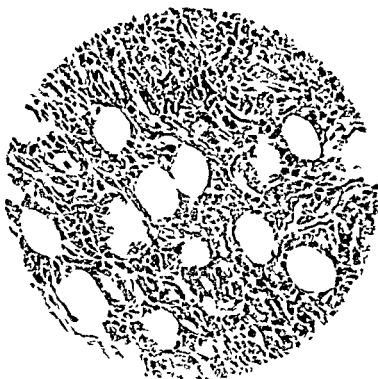


Fig 259—Case II. Photomicrograph showing type of cell and small cystic spaces ( $\times 460$ )

*Note.*—The last case, O. S , died February 17, 1927 of lobar pneumonia No autopsy was permitted.

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### BRANCHIOGENIC TUMORS OF THE NECK

BRANCHIOGENIC tumors of the neck have been a subject of interesting study for many years usually under the title of salivary gland tumors. Three important papers have appeared more recently, those of Wood,<sup>1</sup> Wilson and Willis<sup>2</sup> and McFarland,<sup>3</sup> the latter bringing the number of cases up to 359. These reports agree in attributing to these tumors characteristics of importance to clinicians and pathologists. It seems however that both pathologists and clinicians are in many instances still unfamiliar with this lesion. The various clinical and pathologic diagnoses under which these tumors are found and the equally various treatments applied are proof of the correctness of this statement.

The present small series of 10 cases is reported with the idea of re-emphasizing the importance of these neoplasms. Four of the cases illustrate well the cardinal facts deduced by other writers. The 6 fatal cases all autopsied, bring into relief a feature—or variant—of the group touched on but lightly by them. Whether these 6 are properly called branchiogenic may be open to discussion, but such types must surely be taken into account in diagnoses in the clinic.

I wish to emphasize strongly that the proportion of fatalities in this report is quite uncharacteristic, and is to be attributed to the fact that some 6000 autopsies furnished a goodly proportion of the material searched.

Branchiogenic tumors, as defined (1, 2, 3), are characterized by a location in the lateral aspect of the neck, most often in the parotid region, by a history of long duration, a slow growth (many remain stationary for years) often followed by acceler

ated growth, by a tendency to be cured by local excision (about 70 per cent) or to recur locally (about 30 per cent) and be cured by a second operation (30 per cent of recurrences). The remainder erode and compress locally and a few give rise to distant metastases. The patients are usually between twenty and fifty years of age the sexes are equally represented, the left side slightly more frequently involved. Structurally these tumors are most often of a mixed type showing myxomatous tissue, cellular and hyaline connective tissue and cartilage 'endothelial' cells "indifferent cells and squamous cells in various proportions and combinations. The histologic appearance is that of malignancy. All are not, however demonstrably mixed" for, as McFarland has said all mixed tumors of the neck are branchiogenic but all branchiogenic tumors are not mixed.

Case I—W. McI. a white male sixty three had a tumor on the right side of the neck for an indefinite period which had



Fig. 260—Case I. At time of second recurrence. Branchiogenic adenocarcinoma.

grown considerably shortly before admission to the hospital. No other history was obtained the patient suffering from senile

dementia. The growth, as large as a lemon, was situated over the parotid, pushing up the lobe of the ear. It was circumscribed, freely movable, and at one place showed some fluctuation and ulceration. No primary lesion was found in the mouth or pharynx. A clinical diagnosis of sarcoma of the parotid was made. The mass was excised, the wound healed promptly, and the patient

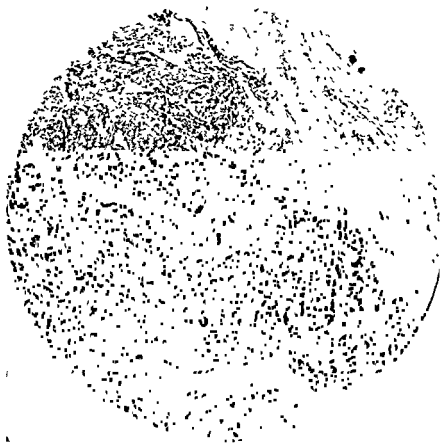


Fig 261 —Case I. A cyst, with papillæ and glands from the second operation

returned to a home for feeble-minded. The histologic diagnosis was mixed tumor. Three years and nine months later the patient was readmitted with a diagnosis of inflammation of the lymph-nodes of the neck. A "gland" was removed, which was diagnosed adenoid basal-cell epithelioma by the pathologist. The wound healed readily and the patient was discharged. He returned a third time nineteen months later showing a large

fluctuating mass at the angle of the jaw (right) a chain of masses from the tip of the mastoid to the supraclavicular fossa, like enlarged lymph nodes and a freely movable blue mass below the first (Fig 260) The blue nodule and the chain of "nodes" were excised and diagnosed, on section adenocarcinoma and metastatic adenocarcinoma respectively The wound healed readily



Fig 262—Case I Area of third biopsy showing adenomatous structure

The patient was given two and a half erythema doses of radium over fourteen weeks and discharged The tumor had not progressed during this time The patient's general condition was good when seen last (February 1927) almost six years after his first operation

A review of the sections showed the first tumor to be a cyst lined by a granulation like tissue in which were large cells not to

be identified. In a crypt of the cyst were a few definite glandular acini. The cyst wall, thick, hyaline fibrous tissue, enclosed islets of small, crowded, round, or oval cells, without other features, evidently the parenchyma of the tumor. Normal parotid gland was attached, but separated by the capsule, except at one place, where, pinched and atrophic, it penetrated well into the capsule. The "gland" removed four years later consisted of a hyaline stroma enclosing small cystic spaces into which projected papillae of connective-tissue and cubic epithelial cells. These cells also formed many definite glandular acini. Some mucoid degeneration of the stroma was noted. Blood-vessels were rare, but hemorrhage into the spaces common (Fig. 261). The last two biopsies were like the second, but cellular elements were in greater preponderance (Fig. 262).

This case represents an adenocarcinoma, primary in the neck. Though no mixed elements were demonstrated, the growth is surely branchiogenic.

**Case II.**—G. C., a white male, sixty-six, three years before admission developed a tumor the size of a pea in the left neck. This had grown rapidly for the preceding four months. He had

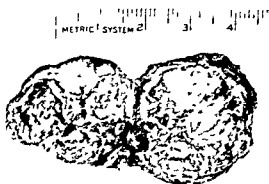


Fig. 263 —Case II. The tumor bisected

no pain, his general condition was good, his hemoglobin 97 per cent. The mass was as large as a walnut, smooth, firm, attached deeply, but not to the skin. No primary lesion was found in the



mouth or pharynx. A diagnosis of branchiogenic tumor was made and the growth removed. The wound healed quickly and the patient referred to the O P D for radiation. The tumor measured 3 x 3 x 3.5 cm. was apparently perfectly encapsulated lobular and elastic. On section it was rather soft, yellowish white except for one brown area. Near the capsule at one point was a gritty structure (Fig. 263). Sections showed the stroma to be dense hyaline abundant and concentrated chiefly under the capsule. Small areas of calcification were numerous. The center of the growth was composed almost entirely of large cells with centrally placed pale nuclei and large nucleoli. There was an abundant cytoplasm. Marked uniformity of cells was noteworthy. They were closely placed with no patterning and with a very little fine fibrillar tissue between groups but not between individual cells. *There were large areas of necrosis.* Blood vessels were scarce except in one small location where a fair number with thin walls were seen. The structure was typically that of so-called endothelioma.

The long preoperative duration of this tumor, the absence of pain and the encapsulation place it in the branchiogenic classification. The histology is consistent although no mixed elements surely appeared. The postoperative duration (five weeks) is of course too short to be of value.

Case III—P. P. a white male fifty ten years prior to admission developed a small lump in the right side of his neck which was followed by a number of such lumps in a chain. He had no sore throat or hoarseness. These masses were removed at another hospital (history and tissues not available) where a diagnosis of carcinoma of the cervical glands was made. The growth recurred about one year later and was removed at another hospital. It recurred a second time and during the last year has grown rather rapidly. When seen he had a series of nodules on the right side of his neck firm movable painless. One was cystic (Fig. 264). Operation was considered inadvisable and up to the present he has received three erythema doses of radium with some regression of the tumor. His general condition re

mains good. A section from the second operation showed a dense fibrous stroma in which were small masses of very anaplastic

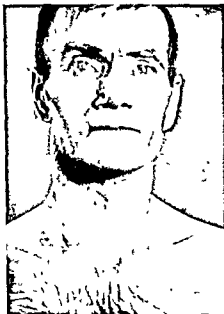


Fig 264—Case III. Second recurrence of branchiogenic tumor. Duration of ten years

squamous cells. These varied in type from basal to horny cells. The growth appeared to be within a lymph-node.

**Case IV.**—J. C., a white male, forty-six, noticed a small, hard, painless lump on his left cheek,  $\frac{1}{2}$  inch anterior to the ear, fifteen months before admission. This grew rapidly to the size of a walnut in four months and became purple. It was then excised by Dr. J. Y. Porter, of Key West, Florida, who made a diagnosis of mixed tumor of the parotid. Recurrence took place, but growth was stopped by heavy radiation. When seen the mass was 3.5 x 1.5 inches (Fig. 265), hard, painless, fixed at the upper part, but movable elsewhere. It did not show internally. There were no enlarged lymph-nodes, and the patient's general condition was good, hemoglobin 82 per cent. A diagnosis of carcinoma of the parotid was made, and radiation again applied, with some improvement. The tumor eventually broke down



Fig. 265—Case IV. Branch of the tumor of parotid gland recurrence one year after operation.



Fig. 266—Case IV.

(Fig 266) and paralysis of the facial nerve developed. The patient is still in the ward with an ulcerated lesion as large as the palm of the hand (Fig 267) His general condition remains good, there is no enlargement of the regional lymph-nodes (two years and nine months after onset)



Fig 267 —Case IV

A biopsy taken on admission from the edge of the lesion showed a typical prickle cell carcinoma eroding approximately normal skin.

These 4 cases comprise the benign group By this is meant cases without characteristics of true malignancy It is realized that all of these may eventually succumb to these tumors The fatal cases follow

Case V.—P P, a white male, sixty-six, noticed a small, painful tumor in the left side of the neck three months prior to admission, which grew rapidly A month later he began to suffer with dizziness, and severe headaches, chiefly on the side of the tumor For one month he has had a severe cough with expectoration of mucus, but no blood The mass measured 10 x 5 cm and extended from a point behind the jaw downward and forward It was stony hard, fixed deeply, but not to the skin.

The tongue protrudes to the left and the left tonsil is enlarged and the posterior pillar pulled toward the midline. No primary growth was found in the mouth. A tumor 5 cm in diameter was found on the sternum. This had been present two months. A Ray showed no involvement of the lungs. A clinical diagnosis of carcinoma of the pharynx with metastases to the submaxillary lymph nodes was made. The patient grew weaker and died four and a half months after onset.

At autopsy the mass was not adherent to the skin but had largely destroyed the sternomastoid muscle and was attached to the larynx and trachea. It was continuous with a mass behind the trachea apparently lymph nodes. The sternum was deeply eroded. The liver, retroperitoneal lymph nodes and pelvic peritoneum showed secondary lesions. Sections showed a loose delicate fibrous stroma enclosing large and small masses of very anaplastic cells. These were generally oval or round, more rarely irregular and spindle shaped, with irregular nuclei and scant cytoplasm. Nucleoli were not prominent. There were large areas of necrosis. Blood vessels were few and well developed. There was no tendency to perivascular grouping of cells. The appearance was that of a sarcoma of endothelial type.

**Case VI—C. McV.** a white male fifty eight developed seven months before admission a lump no larger than a pea under the skin of the right cheek which was movable painless and of rapid growth. On admission he had sharp pain radiating from the growth up behind the ear to the parietal region. He was hoarse and complained of difficulty in swallowing. The mass was the size of a fist, arose apparently from the anterior cervical glands, was hard, nodular and deeply fixed. It was not attached to the skin. Pharynx was observed and found only reddened. There was some general lymphatic enlargement. A clinical diagnosis of carcinoma of the larynx with metastases to the cervical lymph nodes was made. The patient developed diarrhea, grew weaker and died nine months after onset.

At autopsy the tumor consisted of nodular masses, fibrous in appearance with gelatinous areas resembling scirrhous carcinoma.

noma As no mention was made of the lymph nodes it is presumed that the tumor was considered primary in these The tonsils, pharynx, larynx, tongue, prostate, and rectum were examined and found to contain no growth Sections showed an anaplastic growth of endothelioid type in a myxomatoid stroma There were no metastases

Case VII —P M, a white male, forty five, gave a history of onset, dating back four months, of a swelling in the left side of the neck, which was painful and grew rapidly A month later the growth was removed at another hospital The surgeon found it adherent to the carotid sheath and other structures and considered it malignant, the pathologist agreeing, placing it "between sarcoma and carcinoma" It had been located in the center of the neck under the sternomastoid muscle When seen the tumor was 10 x 7 cm, reddish blue, irregular, hard with soft areas and fixed Patient complained of pain and bleeding from the throat A careful examination made before the first operation showed no primary growth in the air passages This examination was repeated in this hospital with similar negative result A diagnosis of carcinoma primary in the epiglottis with metastases to the neck was made The tumor grew, bled often, and the patient grew weaker and died

At autopsy the growth was described as a series of enlarged lymph nodes anterior to the sternomastoid muscle The skin was ulcerated At the base of the epiglottis on the left were three masses the size of a pea, two white and firm, one red and ulcerated Stained sections showed a typical prickly cell carcinoma of both the epiglottis and the mass in the neck This case may be open to question as one of primary cancer of the epiglottis However, I feel that the primary site in the neck was well established by the history and the two careful examinations of the air passages, and that the epiglottis was involved by extension

Case VIII —R H, a white male, fifty seven, noticed a small lump below the left ear, which grew somewhat and was slightly

painful. It was removed at another hospital but regrew in two to three weeks. On admission the entire duration of the lesion was nine months. The mass was as large as two fists, situated under the lobe of the ear and extending downward in the neck. It was hard, uneven and slightly painful. The patient grew gradually weaker, complained of dysphagia and died after an illness of ten months.

Autopsy added nothing to the description of the primary growth. Both lungs showed many metastases. Stained sections of the original tumor showed a moderately cellular stroma in which were masses of cells of an indifferent type suggestive of both squamous cells and endothelial cells. Those from the autopsy material revealed a rather typical endothelioma type of growth with definite perivascular grouping (so called perithelioma).

Case IX—R. G. a white male sixty developed a tumor two weeks before admission below the angle of the jaw over the sternomastoid muscle. When seen it was the size of a hen's egg, firm, uneven, tender and painful. The skin moved freely over it. Tonsils and pharynx were negative. A diagnosis of inoperable carcinoma or sarcoma was made. The patient went down rapidly and died after an illness of five and a half months.

At autopsy the tumor was 9 x 9 cm. of cartilaginous consistency and superficially ulcerated. The esophagus and trachea were not involved. Histologically the structure was that of a squamous cell carcinoma. There were no metastases.

Case X—C. A. a white male sixty three injured the side of his head fourteen months before admission. Several weeks after injury a tumor developed below the right ear which was painful, tender and of rapid growth. This was incised elsewhere. The mass extended well forward from the mastoid and from the upper pole of the parotid a third of the distance down the neck. It was hard in places, soft in others. It was not attached to the skin. A small painful ulceration was found on the inner side of the gum on the right. The lymph nodes of both sides of the neck were

palpable Throat examination revealed only atrophic tonsils The clinical diagnosis was lymphosarcoma The patient lost strength rapidly and died fourteen months after onset

Autopsy revealed metastases to the lungs liver, and kidney Sections showed rather typical endothelioma with tendency to perivascular grouping (perithelioma)

The two groups of this series represent an interesting contrast The first 4 cases, all living in general fit into the definition of branchiogenic tumors given above Six ran a fatal course, 3 with distant metastases Inasmuch as the benign group yield well to local removal (70 per cent cures) but poorly to radiation, and the present tendency is to radiate and not operate many malignant tumors especially lymphomas, it seems very necessary to separate these two groups before beginning treatment This study, and others, it may be remarked have been made chiefly from the standpoint of end results To be of practical use to the clinician such deductions must be made as to permit the application of this knowledge to the patient on his first visit with reasonable hope that the most advantageous course of treatment will be selected It is with this idea in mind that the following tabulations are made

Age Malignant, fifty eight years, benign fifty six years McFarland Malignant (14 cases) fifty-one years and seven months, benign thirty three Wood (chiefly benign) forty years

Preoperative duration Malignant, six months, benign, four months to many years

McFarland Malignant, two years and five months, benign, seven years Wood eight years and nine months

Entire duration Malignant eight and five tenth months, benign, many years, all series

Rapid growth Malignant, 6 cases, benign, 1 McFarland 2 of 10 malignant cases, 16 others showed accelerated growth after a quiescent period, but proved to be benign Wood considered both rapid and accelerated growth as indicative probably of malignancy

Pain Malignant 6 cases, benign 0 McFarland 8 cases of 90 had pain of which 2 were malignant



Hard consistency Malignant 6 cases benign 2 Wood considered hard tumors as probably benign soft ones as probably malignant

Fixation to deep tissues Malignant 4 cases benign 1

Fixation to skin Malignant 0 benign 0 Terminally the malignant growths did invade the skin

Recurrence Malignant 2 benign 2

Dysphagia Malignant 2

Enlargement of regional lymph nodes Malignant 3 Three others were considered primary in the nodes Two of the benign cases were also considered to be lymphadenopathies This would appear to be of little value

The points of contrast then in order of apparent importance are pain rapid growth deep fixation of growth short preoperative duration and an older age incidence in malignant cases These are really the standard criteria of malignant growths in any location The other points seem as characteristic of one group as the other I wish to reemphasize here the observation of McFarland that the histologic appearance can in no wise differentiate between cases which will run a malignant course and those which will run a benign All these cases showed more or less well marked histologic criteria of malignancy Nor is the predominating cell type helpful In this series the endothelioma type appeared in 4 malignant cases squamous cells in 2 The benign group showed endothelioma once adenocarcinoma once and squamous cells twice

Other lesions which might be confused with branchiogenic tumors are first secondary carcinoma of the cervical lymph nodes It would seem sufficient in such cases to demonstrate a primary growth in the areas drained by these nodes Dr Fielding O Lewis is my authority for the statement that malignant growths in these locations may rarely cause no subjective symptoms until after metastases have occurred but that a careful internal examination could hardly fail to detect them Primarily in the tissues of the neck then is the first consideration to be established by history and examination Skin growths squamous cell and basal cell carcinomas are of the skin while branchiogenic tumors

are under the deep fascia, at least for a definite period after onset. Sebaceous cysts are likewise external to the deep fascia. Thyroglossal cysts are in the sagittal line. Of the primary lymphomas, leukemia may be differentiated by the blood-count; lymphosarcoma of the small cell type characteristically shows diffuse involvement of many nodes; Hodgkin's disease is usually more slowly progressive from group to group. Large cell lymphosarcoma (endothelioma) of lymph-nodes offers most difficulty. This does not give a history of long duration, is not cystic as many of the branchiogenic tumors are, is not definitely encapsulated, and usually gives the "feel" of a group of matted nodes. Some cases of branchiogenic tumor, especially recurrent masses, do, however, simulate just such a picture of lymphadenopathy.

Biopsy in the sense of a small piece of tissue should not be practised, as a mixed tumor must generally be demonstrated by study of considerable tissue. Given a resected growth, however, demonstration of a mixed structure suffices to place a given case clearly in the category of branchiogenic tumors. Likewise the finding of an adenocarcinoma, or a squamous-cell growth, surely primary in this site, so classifies the case. There remains a proportion of cases whose histologic structure is indistinguishable from the so-called endotheliomas, and indeed many are so called by competent pathologists following Volkmann's idea. In many of these such clinical features as slow growth, absence of pain, long preoperative duration, etc., will serve to place the case among the branchiogenic growths.

Whether the four malignant cases of endothelioid type here recorded are really branchiogenic or lymphosarcoma of the large cell type I cannot say. All were malignant from the onset, and all fall under the heading of sarcoma. Their preoperative history, I feel, would serve, at any rate, to separate them from the usual type of branchiogenic tumor of benign tendencies, and to indicate treatment by radiation rather than by excision.

All probable branchiogenic tumors, exclusive of those showing the cardinal indications of malignancy, I believe should be wholly excised, with the expectation of about 70 per cent. of primary cures; and recurrent growths likewise removed. Their

histology should be carefully studied with the idea of confirming their branchiogenic origin and as a guide in subsequent treatment. And finally the site should be radiated as an added precaution. This opinion seems justified in the light of present knowledge and until more mature surgical judgment is brought to bear on the subject.

I wish to express sincere appreciation for valuable help and advice given me by Dr. Joseph McFarland in the preparation of this paper.

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